Supplementary material: Search strategy

The search strategy was developed to identify studies on the use of the Molecular Adsorbent Recirculating System (MARS) in trauma-associated acute or acute-on-chronic liver failure, excluding other liver support therapies. The search was conducted across PubMed/MEDLINE, Embase, Cochrane CENTRAL, Scopus, Web of Science, LILACS, ClinicalTrials.gov, and the WHO International Clinical Trials Registry Platform (ICTRP), from inception to March 2025. Manual searches of reference lists from relevant studies were performed to identify additional sources.

The search combined controlled vocabulary (e.g., MeSH, Emtree) and free-text terms, focusing on MARS and trauma-related liver failure. Key terms included:

Intervention: "Molecular Adsorbent Recirculating System," "MARS," "extracorporeal liver support," "artificial liver support"

Condition: "liver failure," "acute liver failure," "acute-on-chronic liver failure," "hepatic failure," "liver injury," "hepatic trauma," "traumatic liver injury," "liver dysfunction," "liver insufficiency"

Context: "trauma," "injury," "injuries," "shock," "hemorrhagic shock"

Search Strings:

PubMed/MEDLINE:("MARS" OR "Molecular Adsorbent Recirculating System" OR "extracorporeal liver support" OR "artificial liver support") AND ("Liver Failure"[Mesh] OR "Hepatic Failure" OR "acute liver failure" OR "acute-on-chronic liver failure" OR "liver injury" OR "hepatic trauma" OR "traumatic liver injury" OR "liver dysfunction" OR "liver insufficiency") AND ("trauma" OR "injury" OR "injuries" OR "shock" OR "hemorrhagic shock")

Embase:('molecular adsorbent recirculating system' OR 'MARS' OR 'extracorporeal liver support' OR 'artificial liver support') AND ('liver failure' OR 'hepatic failure' OR 'acute liver failure' OR 'acute-on-chronic liver failure' OR 'liver dysfunction' OR 'liver insufficiency' OR 'liver injury' OR 'hepatic trauma' OR

'traumatic liver injury') AND ('trauma' OR 'injury' OR 'injuries' OR 'shock' OR 'hemorrhagic shock')

Cochrane CENTRAL:("MARS" OR "Molecular Adsorbent Recirculating System" OR "extracorporeal liver support" OR "artificial liver support") AND ("liver failure" OR "hepatic failure" OR "acute liver failure" OR "acute-on-chronic liver failure" OR "liver injury" OR "hepatic trauma" OR "traumatic liver injury" OR "liver dysfunction" OR "liver insufficiency") AND ("trauma" OR "injur*" OR "shock" OR "hemorrhagic shock") IN Title Abstract Keyword

Scopus:(TITLE-ABS-KEY("MARS" OR "Molecular Adsorbent Recirculating System" OR "extracorporeal liver support" OR "artificial liver support")) AND (TITLE-ABS-KEY("liver failure" OR "acute liver failure" OR "acute-on-chronic liver failure" OR "hepatic failure" OR "liver dysfunction" OR "liver insufficiency" OR "liver injury" OR "hepatic trauma" OR "traumatic liver injury")) AND (TITLE-ABS-KEY("trauma" OR "injury" OR "injuries" OR "shock" OR "hemorrhagic shock"))

Web of Science:('molecular adsorbent recirculating system'/exp OR 'MARS' OR 'extracorporeal liver support' OR 'artificial liver support') AND ('liver failure'/exp OR 'acute liver failure' OR 'acute-on-chronic liver failure' OR 'hepatic failure' OR 'liver dysfunction' OR 'liver insufficiency' OR 'liver injury' OR 'hepatic trauma' OR 'traumatic liver injury') AND ('trauma'/exp OR 'trauma' OR 'injury' OR 'injuries' OR 'shock' OR 'hemorrhagic shock')

ClinicalTrials.gov:

Condition or Disease: liver failure OR hepatic failure OR acute liver failure OR acute-on-chronic liver failure OR liver injury OR traumatic liver injury OR hepatic trauma

Other Terms: MARS OR Molecular Adsorbent Recirculating System OR extracorporeal liver support OR artificial liver support

Study Type: All Studies (Interventional preferred)

Recruitment Status: All Studies

Age: Adult (18+)

First Posted Date: No restriction

WHO ICTRP:

Search: ("MARS" OR "Molecular Adsorbent Recirculating System" OR "extracorporeal liver support" OR "artificial liver support") AND ("liver failure" OR "acute liver failure" OR "acute-on-chronic liver failure" OR "hepatic failure" OR "liver dysfunction" OR "liver injury" OR "traumatic liver injury" OR "hepatic trauma")

Filters: All trials (no restriction)

Age: Adult (optional)

LILACS:(MARS OR "Molecular Adsorbent Recirculating System" OR "extracorporeal liver support" OR "artificial liver support") AND ("liver failure" OR "hepatic failure" OR "acute liver failure" OR "acute-on-chronic liver failure" OR "liver dysfunction" OR "liver insufficiency" OR "liver injury" OR "hepatic trauma" OR "traumatic liver injury") AND ("trauma" OR "injury" OR "shock" OR "hemorrhagic shock")

Supplementary Table 1 Summary of studies investigating molecular adsorbent recirculating system therapy in acute liver failure, with emphasis on trauma-related cases

Ref.	Country	Study Design	Sample Size	Trauma Cases	Context	Year
Ben-Abraham *et al*[3]; 2003	Israel	Case report	1	1	Intensive care unit	2003
Rittler *et al*[4]; 2004	Germany	Observational cohort	5	1	Surgical intensive care unit	2004
Monet *et al*[14]; 2022	France	Observational cohort	180	1	Intensive care unit	2022
Powell *et al*[5]; 2024	USA	Observational cohort	61	8	Trauma/transplant center	2024

Supplementary Table 2 Bias assessment of included studies

Ref.	Study Design	NOS Score (0–9)	Selection Bias	Confounding Bias	Reporting Bias	Implications of Biases	Mitigation Strategies for Future Research
Ben-Abraham *et al*[3]; 2003	Case report (n=1, trauma)	2/9	Critical: Single case, no control group, subjective selection.	Critical: Impossible to adjust for confounders due to study design.	Moderate: Detailed biochemical data, but no long-term outcomes reported.	Positive outcomes may reflect spontaneous recovery or other treatments, not necessarily Molecular Adsorbent Recirculating System. Generalization is impossible.	- Avoid case reports in favor of prospective cohorts. - Include control groups to compare Molecular Adsorbent Recirculating System vs. standard therapy. - Report standardized outcomes (e.g., 30-day survival, liver regeneration).
Rittler *et al*[4]; 2004	Retrospective observational (n=5; 1 trauma)	5/9	High: Only 1 trauma case in a mixed cohort; inclusion criteria not specific to trauma.	High: No adjustment for sepsis severity or liver injury; all patients had MOF.	Moderate: Biochemical data reported, but no details on trauma-specific outcomes.	Predominance of sepsis/MOF masks Molecular Adsorbent Recirculating System effect in trauma. 100% mortality may be due to uncontrolled sepsis, not Molecular Adsorbent Recirculating System failure.	- Exclude patients with persistent sepsis or control for it before Molecular Adsorbent Recirculating System. - Adjust for factors like Multiple Organ Failure score and AAST. - Report trauma-specific outcomes, even in mixed cohorts.
Powell *et al*[5]; 2024	Retrospective observational (n=61; 8 trauma)	7/9	Moderate: Single-center; selection based on MARS access, potentially excluding severe cases.	Moderate: No adjustment for angioembolization or volume resuscitation, which may influence recovery.	Low: Detailed biochemical and clinical outcomes, but no trauma-specific subanalysis.	Reported efficacy may be overestimated due to concurrent interventions. Single-center data limit generalizability.	- Conduct multicenter studies with standardized protocols. - Adjust for concurrent interventions (e.g., angioembolization). - Report subanalyses for trauma cases.
Monet *et al*[14]; 2022	Retrospective observational (n=180; 1 trauma)	5/9	Critical: Only 1 trauma case in a large cohort; inclusion criteria not specific to trauma.	High: No adjustment for etiology or injury severity; mixed cohort with predominantly non-traumatic causes.	Moderate: Aggregated data with no details on the trauma case.	Inclusion of only 1 trauma case precludes trauma-specific conclusions. Mixed data mask Molecular Adsorbent Recirculating System impact in trauma.	- Focus on trauma-exclusive cohorts. - Adjust for etiology and severity (e.g., AAST, ISS). - Report trauma-specific outcomes, even in mixed cohorts.

Supplementary Table 3 Summary of key gaps and recommendations for future research on molecular adsorbent recirculating system in trauma-associated liver failure

Research Area	Gap Identified	Relevant Studies	Recommendations
Trauma-Specific Outcomes	Trauma cases often reported as part of mixed-etiology cohorts, limiting interpretation	(Monet 2022) [14], (Ben-Abraham 2003)[3]	Future studies should report trauma-specific outcomes separately to improve external validity.
Adverse Events	Insufficient reporting on Molecular Adsorbent Recirculating System-related complications, including bleeding and coagulopathy	(Monet 2022)[14], (Ben-Abraham 2003)[3]	Prospective studies should include standardized adverse event reporting, particularly in trauma populations.
Controlled Studies	Lack of randomized controlled trials (RCTs) or comparator groups in trauma settings	All included studies [3–5,14]	Design and conduct RCTs or high-quality cohort studies to evaluate the efficacy and safety of Molecular Adsorbent Recirculating System in trauma patients.

Preferred reporting items for systematic reviews and meta-analyses extension for scoping reviews checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	1-2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	2
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	2
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a	2

		Web address); and if available, provide registration information, including the registration number.	
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	3
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	3
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	15-16
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	3
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	3

Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	3
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	3-4; 17
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	3-4

RESULTS

Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	4-5
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	5
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	5-6; Supl. 2
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	7-8

Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	7-8 Supl 2
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	8-9
Limitations	20	Discuss the limitations of the scoping review process.	9
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	10-11
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	11

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.

† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).

‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.

§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMAScR): Checklist and Explanation. Ann Intern Med. 2018;169:467–473. doi: 10.7326/M18-0850.