Supplementary Material

Literature Search Strategy and Study Selection

Databases and search procedures

Literature searches were conducted to identify evidence on Nrf2–Keap1 signaling, ferroptosis, and pharmacological interventions in ischemic stroke. The sources searched were PubMed/MEDLINE, Scopus, Web of Science Core Collection, ClinicalTrials.gov, and Google Scholar. Publications from 2023 to June 2026 were prioritized, but earlier studies were also considered when relevant to the review objectives. Additional searches addressed individual drug candidates, pharmacokinetics, blood–brain barrier penetration, central nervous system (CNS) exposure, safety, and clinical translation. Reference lists of relevant publications were examined to identify further studies. Across the five sources, 900 records were identified: 248 from PubMed/MEDLINE, 312 from Scopus, 196 from Web of Science Core Collection, 24 from ClinicalTrials.gov, and 120 from Google Scholar. After 215 duplicates were removed, 685 records remained. Initial screening excluded 548 records, leaving 137 full-text reports for eligibility assessment. Of these, 67 were excluded, leaving 70 references for the final review.

The following search combinations were used for the respective databases to identify literature on ischemic stroke, Nrf2–Keap1 signaling, ferroptosis, and related pharmacological and translational aspects

Database	Search strategy
PubMed/MEDLINE	("Stroke"[Mesh] OR "Brain Ischemia"[Mesh] OR stroke*[tiab] OR "ischemic stroke"[tiab] OR "ischaemic stroke"[tiab] OR "cerebral ischemia"[tiab] OR "cerebral ischaemia"[tiab] OR "brain ischemia"[tiab] OR "ischemic brain injury"[tiab] OR "ischemia-reperfusion"[tiab] OR "ischemia-reperfusion injury"[tiab]) ("NF-E2-Related Factor 2"[Mesh] OR Nrf2[tiab] OR "Nrf-2"[tiab] OR "nuclear factor erythroid 2-related factor 2"[tiab] OR Keap1[tiab] OR "Kelch-like ECH-associated protein 1"[tiab] OR "Nrf2-Keap1"[tiab] OR "Nrf2/Keap1"[tiab]) (ferroptos*[tiab] OR "lipid peroxidation"[tiab] OR "glutathione peroxidase 4"[tiab] OR GPX4[tiab] OR SLC7A11[tiab] OR "system Xc-"[tiab] OR ACSL4[tiab] OR ferritinophagy[tiab] OR "iron homeostasis"[tiab])
Scopus	((stroke* OR "ischemic stroke" OR "ischaemic stroke" OR "cerebral ischemia" OR "cerebral ischaemia" OR "brain ischemia" OR "ischemia-reperfusion injury") AND (Nrf2 OR "Nrf-2" OR Keap1 OR "Nrf2-Keap1" OR "Nrf2/Keap1" OR "nuclear factor erythroid 2-related factor 2") AND (ferroptos* OR "lipid peroxidation" OR GPX4 OR SLC7A11 OR ACSL4 OR ferritinophagy OR "iron homeostasis" OR "system Xc-"))
Web of Science Core Collection	((stroke* OR "ischemic stroke" OR "ischaemic stroke" OR "cerebral ischemia" OR "cerebral ischaemia" OR "brain ischemia" OR "ischemia-reperfusion injury") AND (Nrf2 OR "Nrf-2" OR Keap1 OR "Nrf2-Keap1" OR "Nrf2/Keap1" OR "nuclear factor erythroid 2-related factor 2") AND (ferroptos* OR "lipid peroxidation" OR GPX4 OR SLC7A11 OR ACSL4 OR ferritinophagy OR "iron homeostasis" OR "system Xc-"))
ClinicalTrials.gov	1. Ischemic stroke AND ferroptosis 2. Ischemic stroke AND Nrf2 3. Ischemia–reperfusion AND oxidative stress 4. Ischemic stroke and candidate interventions, including edaravone and dimethyl fumarate
Google Scholar	1. "ischemic stroke" Nrf2 Keap1 ferroptosis 2. "ischemia-reperfusion injury" Nrf2 ferroptosis 3. "ferroptosis" "ischemic stroke" pharmacological 4. "blood-brain barrier" Nrf2 stroke drug repurposing

Eligibility criteria

Criterion	Included	Excluded
Disease relevance	Ischemic stroke, cerebral ischemia, or ischemia–reperfusion injury	Studies unrelated to the review's disease or translational questions
Molecular mechanisms	Nrf2–Keap1 signaling, ferroptosis, oxidative stress, or related mechanisms	Studies without a meaningful connection to the review objectives
Interventions	Relevant pharmacological agents, drug repurposing, and drug-delivery approaches	Interventions with no relevant mechanistic or translational contribution
Pharmacology and translation	Pharmacokinetics, CNS exposure, blood–brain barrier penetration, safety, and clinical evidence	Studies that do not inform the pharmacological or translational questions
Study type	Relevant experimental studies, clinical investigations, reviews, and meta-analyses	Editorials or other publications lacking relevant supporting evidence
Other disease models	Studies providing relevant mechanistic or pharmacological information	Studies whose findings could not reasonably inform the review questions
Reporting	Publications providing sufficient information to interpret the relevant findings	Publications lacking sufficient relevant information

Evidence from diseases other than ischemic stroke was considered indirect and was not interpreted as proof of efficacy in stroke.