American Journal of Forensic Psychology
ISSN: 0733-1290

https://doi.org/10.61336/AJFP/2026-1-28 https://americanforensicpsychology.org/index.php/ajfp/index

Original Research Article

Effect of Hypothermia Physiology on Drug Metabolism and Toxicity in Forensic Cases: A Narrative Scoping Review and Interpretive Framework.

Name of Author:

Dr. Jaswinder Singh[1]*, Dr. Harsharan Kaur Billawria[2].

Affiliation:

[1]Associate Professor, Deptt of Forensic Medicine, RIMT Medical College, Mandi Gobindgarh, Distt. Fateh Garh Sahib Punjab.

[2]MD Physiology Associate Professor Department of Physiology RIMT Medical College Mandi Gobindgarh Distt. Fateh Garh Sahib punjab

Corresponding Author: Dr. Jaswinder Singh.

E-Mail: dr.harsharankaur1962@gmail.com

Received: 26-06-2026
Revised: 09-06-2026
Accepted: 27-06-2026
Published: 08-07-2026

Abstract: ***Background:*** Background: Hypothermia is a clinically and forensically important physiological state in which reduced core body temperature alters cardiovascular function, hepatic enzyme activity, renal clearance, tissue perfusion, protein binding, and central nervous system responsiveness. In forensic cases, these changes may modify both the actual toxicity of drugs during life and the interpretation of postmortem drug concentrations after death. ***Aim:*** To evaluate the effect of hypothermia physiology on drug metabolism, drug toxicity, and postmortem toxicological interpretation in forensic cases, with emphasis on mechanisms relevant to alcohol, sedatives, opioids, antidepressants, antipsychotics, cardiovascular drugs, and polypharmacy. ***Methodology:*** A narrative scoping review was conducted using published literature from forensic toxicology, clinical pharmacokinetics, targeted temperature management, accidental hypothermia, postmortem redistribution, and drug-related death interpretation. Evidence was synthesized into mechanistic domains: absorption, distribution, metabolism, excretion, pharmacodynamic sensitivity, postmortem redistribution, and forensic interpretation. The results are presented as seven structured tables with interpretive inferences. ***Results:*** Hypothermia reduces hepatic enzymatic metabolism, particularly temperature-dependent cytochrome P450-mediated biotransformation; decreases hepatic and renal blood flow; delays gastrointestinal absorption; alters protein binding and tissue distribution; and increases pharmacodynamic vulnerability to central nervous system and respiratory depressants. These effects are especially important for opioids, benzodiazepines, sedative-hypnotics, antidepressants, antipsychotics, ethanol, and drugs with narrow therapeutic indices. Postmortem interpretation is complicated by redistribution, sampling-site variability, impaired premortem metabolism, delayed clearance, decomposition, and overlap between hypothermia biomarkers and drug or ethanol effects. ***Conclusion:*** Hypothermia should be considered an active modifier of drug toxicity rather than a passive background condition. In forensic cases, a drug concentration that appears therapeutic or borderline toxic under normothermic assumptions may become lethal in the presence of hypothermia-induced metabolic suppression, impaired clearance, altered consciousness, and respiratory depression. Interpretation should integrate scene findings, core-temperature history where available, autopsy findings, vitreous biochemistry, peripheral blood toxicology, drug class, tolerance, comorbidity, and postmortem interval.

Keywords: Hypothermia; forensic toxicology; drug metabolism; postmortem redistribution; cytochrome P450; drug toxicity; ethanol; opioids; benzodiazepines; accidental death.

INTRODUCTION

Hypothermia is generally defined as a fall in core body temperature below 35°C. In forensic practice, fatal hypothermia is encountered in outdoor exposure, homelessness, intoxication, drowning, neglect, elderly deaths, psychiatric illness, immobilization, trauma, and drug-related deaths. The diagnosis is often difficult because autopsy findings may be absent, subtle, or nonspecific. Classical findings such as Wischnewsky spots, pancreatic changes, renal tubular changes, frost erythema, paradoxical undressing, or terminal burrowing are supportive but not pathognomonic. Recent forensic literature has therefore emphasized the need for combined interpretation using scene findings, autopsy, histology, toxicology, vitreous chemistry, and emerging biomarker approaches.1,2

Drug metabolism and toxicity are temperature-sensitive biological processes. Hypothermia reduces enzymatic reaction rates, modifies organ perfusion, delays gastrointestinal motility, impairs renal elimination, changes tissue distribution, and alters receptor-level drug response. These effects are clinically recognized in patients undergoing therapeutic or targeted temperature management, where sedatives, opioids, anticonvulsants, neuromuscular blockers, antimicrobials, and cardiovascular drugs may show altered pharmacokinetics.3,4 In forensic cases, similar principles may apply, but interpretation is more complex because the toxicologist is usually reconstructing events after death rather than monitoring concentrations during life.

A central problem is that postmortem drug concentration is not always equivalent to the antemortem concentration at the time of death. Postmortem redistribution, sample-site variation, tissue diffusion, residual metabolism, decomposition, bacterial activity, and drug instability may all alter measured concentrations. 5,6 Hypothermia adds another layer of complexity: it may increase toxicity during life by slowing metabolism and clearance, while also slowing some postmortem processes after death. Therefore, hypothermia can influence both the biological pathway to death and the evidentiary interpretation of toxicology results.

This article reviews the physiological mechanisms by which hypothermia affects drug metabolism and toxicity and proposes a forensic interpretation framework for deaths involving cold exposure, intoxication, or both.

Aim and Objectives

Aim

To study the effect of hypothermia physiology on drug metabolism and toxicity in forensic cases.

Objectives

1) To describe the physiological changes of hypothermia relevant to drug absorption, distribution, metabolism, and excretion.
2) To identify drug classes most affected by hypothermia-induced metabolic and pharmacodynamic changes.
3) To evaluate how hypothermia modifies interpretation of postmortem toxicology.
4) To compare the findings with recent forensic and clinical pharmacokinetic studies.
5) To propose a practical forensic interpretation framework for hypothermia-associated drug deaths.

METHODOLOGY

Study Design

This article was designed as a narrative scoping review and interpretive synthesis. The approach was selected because the subject overlaps clinical pharmacology, forensic pathology, forensic toxicology, emergency medicine, and postmortem biochemistry, and because direct prospective forensic studies are ethically and practically limited.

Literature Search Strategy

Published literature was reviewed from the following domains:

- forensic toxicology and postmortem drug redistribution;
- accidental and fatal hypothermia;
- targeted temperature management and therapeutic hypothermia;
- cytochrome P450 enzyme activity under hypothermic conditions;
- ethanol, opioid, benzodiazepine, antidepressant, antipsychotic, and mixed-drug deaths;
- vitreous glucose, beta-hydroxybutyrate, metabolomics, and immunohistochemical markers of hypothermia.

Search terms included: hypothermia and drug metabolism, hypothermia and forensic toxicology, hypothermia and postmortem redistribution, therapeutic hypothermia pharmacokinetics, cytochrome P450 hypothermia, fatal hypothermia toxicology, ethanol hypothermia death, opioid hypothermia, benzodiazepine hypothermia, and postmortem drug concentration interpretation.

Inclusion Criteria

Studies and reviews were included if they addressed one or more of the following:

1) hypothermia-related physiological changes affecting drug kinetics;
2) pharmacokinetic changes during therapeutic or accidental hypothermia;
3) forensic interpretation of postmortem drug concentrations;
4) postmortem redistribution and sampling-site variability;
5) biomarkers or ancillary findings used in hypothermia diagnosis;

6) drug classes commonly encountered in hypothermia-associated deaths.

Exclusion Criteria

Articles were excluded if they were unrelated to human or forensic interpretation, lacked relevance to drug metabolism or toxicity, or were purely experimental without translational relevance.

Data Extraction and Synthesis

Data were extracted into seven thematic categories:

1) physiological changes in hypothermia;
2) ADME effects;
3) drug-class vulnerability;
4) toxicodynamic interactions;
5) postmortem interpretation issues;
6) ancillary forensic markers;
7) practical interpretation framework.

No pooled meta-analysis was attempted because the available literature is heterogeneous in design, temperature range, drug class, population, and outcome measure.

RESULTS

Table 1. Physiological Changes in Hypothermia Relevant to Drug Toxicity

Physiological change	Mechanism	Forensic relevance	Expected effect on toxicity
Reduced cardiac output	Bradycardia, myocardial depression, peripheral vasoconstriction	Reduced organ perfusion and delayed clearance	Increased persistence of active drug
Reduced hepatic blood flow	Cold-induced vasoconstriction and low cardiac output	Lower delivery of drug to liver	Reduced hepatic clearance
Reduced CYP450 activity	Temperature-dependent enzymatic slowing	Particularly relevant for CYP3A, CYP2C, CYP2D, CYP2E1 substrates	Increased parent-drug concentration
Reduced renal perfusion	Vasoconstriction and reduced glomerular filtration	Important for renally cleared drugs	Prolonged elimination half-life
Delayed gastric emptying	Reduced gastrointestinal motility	Tablets may remain in stomach longer	Delayed or prolonged absorption
Altered plasma protein binding	Acidosis, cold stress, altered albumin binding	Free drug may differ from total measured drug	Increased active free fraction in some cases
CNS depression	Reduced neuronal activity and impaired consciousness	Overlaps with sedative and opioid effects	Additive coma and respiratory depression
Coagulopathy and acidosis	Severe hypothermia impairs coagulation and metabolism	May coexist with trauma or intoxication	Increased vulnerability to death

Inference: Hypothermia creates a physiological environment in which drug clearance is reduced and pharmacodynamic vulnerability is increased. Death may occur at concentrations that would not necessarily be fatal in a normothermic, healthy individual.

Table 2. Effect of Hypothermia on Absorption, Distribution, Metabolism, and Excretion

Pharmacokinetic phase	Hypothermic effect	Drug examples	Forensic implication
Absorption	Delayed gastric emptying and reduced gut motility	Ethanol, tablets, sedatives, antidepressants	Stomach contents may contain significant residual drug
Absorption	Reduced peripheral perfusion	Transdermal fentanyl, injected drugs	Slower initial absorption but possible later release during rewarming
Distribution	Peripheral vasoconstriction	Lipophilic sedatives, opioids	Central compartment concentrations may not reflect tissue burden
Distribution	Altered tissue binding	Antidepressants, antipsychotics	Greater redistribution uncertainty
Metabolism	Reduced hepatic enzyme activity	Benzodiazepines, opioids, antidepressants	Parent drug may accumulate
Metabolism	Reduced formation of	Diazepam, amitriptyline,	Parent/metabolite ratios may be

	metabolites	codeine, tramadol	atypical
Excretion	Reduced renal blood flow and filtration	Lithium, gabapentin, pregabalin, digoxin	Increased risk of accumulation
Excretion	Reduced biliary clearance	Some antipsychotics and opioids	Prolonged drug persistence

Inference: Hypothermia affects all major pharmacokinetic phases, but the most forensically important effects are reduced metabolism, reduced clearance, delayed absorption, and abnormal parent/metabolite relationships.

Table 3. Drug Classes Most Affected by Hypothermia in Forensic Cases

Drug class	Main hypothermia-related concern	Mechanism	Forensic significance
Ethanol	Promotes heat loss and impaired judgment	Peripheral vasodilation, reduced shivering, CNS depression	Common cofactor in exposure deaths
Opioids	Respiratory depression worsened by hypothermia	Reduced clearance and reduced ventilatory drive	Fatality may occur at lower concentrations
Benzodiazepines	Sedation, immobility, impaired escape	CNS depression and prolonged half-life	Often contributory rather than sole cause
Z-drugs	Confusion, amnesia, impaired thermoregulation	CNS depression	Risk of exposure and accidental death
Antidepressants	Arrhythmia, CNS depression, redistribution	High volume of distribution, CYP metabolism	Postmortem interpretation difficult
Antipsychotics	Sedation and impaired thermoregulation	Dopamine blockade, anticholinergic effect, CYP metabolism	May predispose to cold exposure death
Barbiturates	Profound CNS and respiratory depression	Enzyme metabolism and narrow safety margin	High lethality in cold exposure
Cardiovascular drugs	Bradycardia, hypotension, conduction defects	Reduced clearance and direct cardiac effects	Hypothermia may magnify arrhythmic risk
Lithium	Renal clearance impairment	Reduced GFR and dehydration	Toxicity may worsen during exposure
Stimulants	Variable effect; exhaustion after agitation	Catecholamine surge followed by collapse	May mask early hypothermia but increase cardiac risk

Inference: Sedative, opioid, psychotropic, cardiovascular, and renally cleared drugs are particularly important in hypothermia-associated deaths. Their toxicity is influenced not only by concentration but also by immobility, impaired judgment, respiratory suppression, and inability to seek warmth.

Table 4. Hypothermia and Parent Drug/Metabolite Interpretation

Pattern observed	Possible hypothermia explanation	Alternative explanation	Interpretation caution
High parent drug with low metabolite	Reduced hepatic metabolism	Acute ingestion shortly before death	Do not assume acute overdose without scene correlation
Therapeutic parent concentration with death	Increased pharmacodynamic sensitivity	Natural disease, tolerance variation	Therapeutic range may not exclude contribution
Low metabolite/parent ratio	CYP inhibition by hypothermia or co-drug	Genetic polymorphism or drug interaction	Consider temperature, genotype, inhibitors
Persistent drug despite survival	Reduced clearance	Repeated dosing	Review prescription history

interval			
Significant gastric residue	Delayed gastric emptying	Recent ingestion	May indicate prolonged absorption
Multiple CNS depressants at modest levels	Additive toxicity under hypothermia	Polypharmacy alone	Combined effect may be lethal
Low ethanol with severe impairment	Reduced tolerance, hypothermic CNS depression	Postmortem ethanol change	Interpret ethanol with vitreous and scene findings

Inference: Hypothermia can produce atypical toxicological patterns that mimic acute overdose, impaired metabolism, or drug interaction. Parent/metabolite ratios should be interpreted cautiously.

Table 5. Postmortem Toxicological Challenges in Hypothermia-Associated Deaths

Challenge	Mechanism	Best practice
Postmortem redistribution	Drug movement from organs into blood after death	Prefer femoral/peripheral blood
Central vs peripheral variation	Cardiac blood more affected by redistribution	Compare sampling sites if available
Delayed cooling or freezing	Environmental temperature affects decomposition	Record body recovery conditions
Residual metabolism after death	Some biochemical activity may persist briefly	Interpret with postmortem interval
Drug instability	Degradation or formation after death	Use validated storage and analysis
Ethanol confounding	Ethanol affects thermoregulation and biomarkers	Compare blood, vitreous, urine if available
Decomposition	Putrefaction may alter concentrations	Use alternative matrices where possible
Tolerance	Chronic users may tolerate high concentrations	Review medical and prescription history
Polypharmacy	Additive or synergistic toxicity	Avoid single-drug interpretation

Inference: A single numerical drug concentration is insufficient in hypothermia-associated deaths. Interpretation requires matrix selection, sampling site documentation, postmortem interval, scene findings, and pharmacological context.

Table 6. Ancillary Findings Supporting Hypothermia Diagnosis and Toxicology Interpretation

Ancillary finding	Sample/source	Interpretation	Limitation
Wischnewsky spots	Gastric mucosa	Supportive of hypothermia	Not always present
Pancreatic or renal tubular changes	Histology	Supportive tissue stress marker	Nonspecific
Vitreous glucose	Vitreous humour	May be elevated in hypothermia	Diabetes and stress confound
Vitreous beta-hydroxybutyrate	Vitreous humour	Suggests cold stress/starvation ketosis	Ethanol may confound
Combined vitreous glucose + BHB	Vitreous humour	Improves diagnostic support	Not independently diagnostic
Toxicology panel	Peripheral blood, urine, vitreous	Identifies contributing drugs	Concentration interpretation complex

Scene evidence	Environment, clothing, shelter, alcohol containers	Essential for diagnosis	May be incomplete
Metabolomic markers	Blood or tissue	Emerging diagnostic support	Not yet routine
Immunohistochemistry	Tissue	Potential future marker	Literature remains fragmented

Inference: Ancillary tests strengthen the diagnosis of hypothermia but cannot replace holistic forensic interpretation. Vitreous chemistry and toxicology are especially valuable when scene evidence and autopsy findings are limited.

Table 7. Proposed Forensic Interpretation Framework

Step	Question	Practical action
1	Was there credible cold exposure?	Review scene, weather, clothing, shelter, heating, immersion, immobilization
2	Was hypothermia physiologically plausible?	Assess age, illness, intoxication, trauma, malnutrition, psychiatric disease
3	Are autopsy findings supportive?	Look for gastric hemorrhages, pancreatic changes, frost erythema, injuries
4	Are ancillary markers supportive?	Examine vitreous glucose, BHB, electrolytes, histology, metabolomics if available
5	Were drugs present?	Use broad toxicology screening, including alcohol and sedatives
6	Could drugs impair thermoregulation or escape?	Assess CNS depressants, antipsychotics, ethanol, opioids
7	Could hypothermia increase drug toxicity?	Consider reduced metabolism, reduced clearance, respiratory depression
8	Is postmortem redistribution likely?	Prefer femoral blood and compare matrices
9	Is concentration alone sufficient?	Avoid isolated interpretation; integrate all evidence
10	What is the most defensible cause-of-death formulation?	Consider “hypothermia with drug contribution,” “mixed drug toxicity with hypothermia,” or combined cause

Inference: The most defensible forensic conclusion is reached when hypothermia and drug toxicity are interpreted as interacting mechanisms rather than competing explanations.

DISCUSSION

Hypothermia modifies drug toxicity through both pharmacokinetic and pharmacodynamic mechanisms. Tortorici et al.3 emphasized that therapeutic hypothermia alters drug disposition, metabolism, and response, particularly through temperature-dependent effects on cytochrome P450 activity. This supports the present synthesis that hepatic metabolism is one of the most important pathways by which hypothermia increases drug persistence. Crombez and Hachimi Idrissi 4 systematically reviewed pharmacokinetics during targeted temperature management after cardiac arrest and concluded that temperature management may affect drug pharmacokinetics in clinically relevant ways. Although their focus was clinical rather than forensic, the principles apply directly to forensic reconstruction: if a drug’s clearance is reduced during controlled cooling in hospital settings, similar or greater disruption may occur during accidental hypothermia complicated by shock, dehydration, ethanol intake, trauma, or immobility.

Experimental work on cardiac arrest and hypothermia has shown isoform-specific reductions in metabolic activity involving CYP3A, CYP2C, CYP2D, and CYP2E pathways.7-9 These pathways are forensically important because they metabolize many opioids, benzodiazepines, antidepressants, antipsychotics, anticonvulsants, and ethanol-related substrates. A high parent-drug concentration with lower-than-expected metabolite concentration may therefore represent hypothermia-related metabolic suppression, acute ingestion, genetic polymorphism, or drug-drug interaction. The interpretation should not rely on the ratio alone.10-12. Stephenson et al.5 highlighted that postmortem toxicology is affected by postmortem redistribution, diffusion, site-to-site variability, drug properties, metabolism, bacterial activity, genetic polymorphism, tolerance, resuscitation, and mixed-drug toxicity. This is highly relevant to hypothermia deaths because many such cases involve multiple confounders: alcohol exposure, delayed discovery, environmental cooling, psychiatric medication, chronic disease, or decomposition. The present review agrees with their position that postmortem concentrations must not be treated as direct substitutes for antemortem concentrations.

Abdelaal et al.6 reviewed postmortem redistribution and

noted the importance of drug properties such as lipophilicity, protein binding, volume of distribution, and sampling site. This is particularly important for antidepressants and antipsychotics, which are commonly encountered in deaths involving exposure, psychiatric illness, or impaired self-care. In such cases, a peripheral concentration may still be more reliable than central blood, but even peripheral blood must be interpreted with caution.

Mack et al.8 demonstrated that vitreous glucose and beta-hydroxybutyrate may assist the diagnosis of hypothermia and that ethanol confounds interpretation. Their findings are important because ethanol is one of the most common substances in hypothermia deaths. Ethanol may promote heat loss through vasodilation, impair shivering, reduce judgment, cause immobility, and intensify CNS depression. Therefore, ethanol can be both a physiological contributor to hypothermia and a confounder of biochemical markers.

Tomassini et al.1 reviewed immunohistochemical approaches to hypothermia diagnosis and concluded that the literature remains fragmented and lacks robust statistical validation. This reinforces the need for cautious interpretation. Immunohistochemistry may support diagnosis in selected cases, but it cannot yet provide a stand-alone diagnostic test for fatal hypothermia.

A large Swedish postmortem metabolomics study identified biomarker patterns associated with hypothermia using forensic autopsy material.2 This suggests that future forensic diagnosis may become more objective, especially in cases where scene evidence is incomplete. However, metabolomic approaches are not yet universally available and must be validated across populations, postmortem intervals, storage conditions, and toxicological contexts.

The present synthesis indicates that hypothermia and drug toxicity should not be viewed as mutually exclusive causes of death. In many cases, the appropriate interpretation may be combined. For example, ethanol and benzodiazepines may not independently reach fatal concentrations, but together they may impair consciousness and prevent escape from a cold environment. Opioids may suppress respiration, while hypothermia further depresses respiratory drive and cardiac function. Antipsychotics may impair thermoregulation and cause sedation, while hypothermia reduces clearance and increases arrhythmia risk. Cardiovascular drugs may become more dangerous when hypothermia induces bradycardia, conduction disturbance, hypotension, or electrolyte shifts. The phrase "therapeutic concentration" must also be used carefully in forensic hypothermia. Therapeutic ranges are generally derived from living, normothermic patients and may not apply to cold, acidotic, immobilized, elderly, malnourished, intoxicated, or comorbid individuals. A concentration below the usual fatal range does not exclude contribution to death. Conversely, a high postmortem concentration does not automatically prove overdose because redistribution and sampling-site variation may exaggerate measured values.13-15

From a medicolegal perspective, the best conclusion should express mechanism and contribution. Depending on the totality of evidence, cause of death may be certified as "hypothermia with contributory mixed-drug toxicity," "mixed-drug toxicity complicated by cold exposure," "ethanol intoxication and hypothermia," or "combined effects of hypothermia and drug intoxication." The wording should reflect whether cold exposure, drug effect, or both were necessary components of the fatal sequence.

Practical Forensic Implications

1) Hypothermia should be treated as a modifier of drug toxicity.
2) Peripheral blood should be preferred for postmortem drug interpretation.
3) Toxicology should include ethanol, sedatives, opioids, antidepressants, antipsychotics, and cardiovascular drugs.
4) Parent/metabolite ratios should be interpreted cautiously.
5) Vitreous glucose and beta-hydroxybutyrate may support hypothermia diagnosis but are not definitive.
6) Ethanol is both a risk factor for hypothermia and a confounder in biochemical interpretation.
7) Therapeutic drug concentrations may still be contributory in hypothermic deaths.
8) Polypharmacy should be interpreted in terms of additive physiological impairment.
9) The final opinion should integrate scene, autopsy, toxicology, histology, biochemistry, and postmortem interval.
10) Combined cause-of-death formulations are often more defensible than single-cause conclusions.

Limitations

This article is a narrative scoping review and not a pooled meta-analysis. The available literature is heterogeneous, with differences in population, drug class, temperature range, clinical versus forensic setting, sampling site, postmortem interval, and analytical method. Direct human forensic studies are limited. Many mechanistic conclusions are extrapolated from therapeutic hypothermia, animal studies, clinical pharmacokinetics, and general postmortem toxicology principles. Therefore, the proposed framework should be used as an interpretive aid rather than a rigid diagnostic rule.

CONCLUSION

Hypothermia has a significant effect on drug

metabolism and toxicity in forensic cases. It reduces hepatic enzyme activity, lowers hepatic and renal blood flow, delays absorption, alters distribution, impairs elimination, and increases pharmacodynamic sensitivity to sedatives, opioids, ethanol, psychotropic drugs, and cardiovascular agents. These changes may transform otherwise therapeutic or borderline toxic concentrations into fatal contributors. In forensic practice, hypothermia-associated drug deaths require integrated interpretation. The toxicological result should not be assessed in isolation. Scene evidence, autopsy findings, peripheral blood concentrations, alternative matrices, vitreous biochemistry, drug class, tolerance, comorbidity, and postmortem redistribution must all be considered. The most accurate medicolegal conclusion often recognizes hypothermia and drug toxicity as interacting and mutually reinforcing mechanisms.

REFERENCES

1. Tomassini L, Lancia M, Gambelunghe C, Ricchezze G, Fedeli P, Cingolani M, et al. Immunohistochemical insights into hypothermia-related deaths: a systematic review. Forensic Sci Med Pathol. 2024;20:1-12.
2. Ahlner J, Green H, Druid H, Holmgren A, Zackrisson AL, Carlsson B, et al. Biomarker patterns and mechanistic insights into hypothermia from a postmortem metabolomics investigation. Sci Rep. 2024;14:1-12.
3. Tortorici MA, Kochanek PM, Poloyac SM. Effects of hypothermia on drug disposition, metabolism, and response: a focus of hypothermia-mediated alterations on the cytochrome P450 enzyme system. Crit Care Med. 2007;35:2196-204.
4. Crombez T, Hachimi Idrissi S. The influence of targeted temperature management on the pharmacokinetics of drugs administered during and after cardiac arrest: a systematic review. Acta Clin Belg. 2017;72(2):116-22.
5. Stephenson L, Van Den Heuvel C, Scott T, Byard RW. Difficulties associated with the interpretation of postmortem toxicology. J Anal Toxicol. 2024;48(6):405-12.
6. Abdelaal GMM, Hegazy NI, Etewa RL, Elmesallamy GEA. Postmortem redistribution of drugs: a literature review. Forensic Sci Med Pathol. 2024;20:1483-90.
7. Fritz HG, Holzmayr M, Walter B, Moeritz KU, Lupp A, Bauer R. The effect of mild hypothermia on plasma fentanyl concentration and biotransformation in juvenile pigs. Anesth Analg. 2005;100(4):996-1002.
8. Mack T, Parai JL, Milroy CM. Establishing vitreous glucose and beta-hydroxybutyrate thresholds to assist in the diagnosis of hypothermia. Forensic Sci Int. 2024;358:111963.
9. Ito H, Hosomi S, Nishida T, Nakamura Y, Iba J, Ogura H, et al. A review on targeted temperature management for cardiac arrest and traumatic brain injury. Front Neurosci. 2024;18:1397300.
10. Stommel AM, Matzneller P, Al Jalali V, Wulkersdorfer B, Lackner E, Mueller M, et al. Impact of hypothermic temperature control on plasma and soft tissue pharmacokinetics of penicillin/beta-lactamase inhibitor combinations in patients resuscitated after cardiac arrest. Clin Pharmacokinet. 2025;64:1-13.
11. Hilberg T, Ripel A, Slørdal L, Bjorneboe A, Morland J. The extent of postmortem drug redistribution in a rat model. J Forensic Sci. 1999;44(5):956-62.
12. Pounder DJ, Jones GR. Post-mortem drug redistribution: a toxicological nightmare. Forensic Sci Int. 1990;45(3):253-63.
13. Drummer OH. Postmortem toxicology of drugs of abuse. Forensic Sci Int. 2004;142(2-3):101-13.
14. Karch SB. Postmortem toxicology of abused drugs. Boca Raton: CRC Press; 2008.
15. Byard RW. Forensic issues in cases of hypothermia. Forensic Sci Med Pathol. 2018;14(3):381-6.