Black Sea Journal of Engineering and Science
doi: 10.34248/bsengineering.1861324

Open Access Journal
e-ISSN: 2619 – 8991

Research Article
Volume 9 - Issue 3: 1432-1443 / May 2026

POSTMORTEM REDISTRIBUTION OF TETRAHYDROCANNABINOL: A DATA RECONSTRUCTION COMPARISON OF CONTROLLED ANIMAL MODELS AND HUMAN CASEWORK

İsmail Ethem GÖREN[1,2,*]

[1]*Ankara University, Institute of Forensic Sciences, Department of Forensic Toxicology, 06620, Ankara, Türkiye*
[2]*Ankara University, Integrated Technologies Research Center (BÜTAM), 06790, Ankara, Türkiye*

Abstract: Postmortem redistribution of tetrahydrocannabinol (THC) remains controversial because controlled animal experiments often show pronounced central-to-peripheral concentration gradients, whereas human casework exhibits highly variable patterns. This study applied retrospective data reconstruction to compare the central-to-peripheral blood ratio of THC and its metabolites between animal models and human forensic casework and to test whether postmortem interval explains the observed variability. A raw dataset was reconstructed from peer-reviewed literature, comprising paired central and peripheral measurements from porcine and rabbit models and a large set of paired measurements from autopsy caseworks. Central-to-peripheral ratios were calculated from matched cardiac and femoral blood concentrations, and nonparametric group comparisons and correlation analyses were performed. Animal models showed consistently elevated central-to-peripheral ratios, whereas human casework clustered near unity with frequent values below 1.0. In animal models, postmortem interval was strongly associated with increasing central-to-peripheral ratio, but no such relationship was observed in human casework. In contrast to THC, the central-to-peripheral ratio for the major carboxy metabolite was near 1.0 in both cohorts. These findings indicate that controlled animal models may overestimate the magnitude and predictability of postmortem redistribution for THC in real-world forensic settings and support interpretation strategies that prioritize peripheral sampling and metabolite context when assessing postmortem cannabinoid results.

Keywords: Postmortem redistribution, Tetrahydrocannabinol, Animal models, Autopsy, Forensic toxicology, Data reconstruction

***Corresponding author:** Ankara University, Institute of Forensic Sciences, Department of Forensic Toxicology, 06620, Ankara, Türkiye
E mail: iegoren@ankara.edu.tr (İ. E. GÖREN)
İsmail Ethem GÖREN https://orcid.org/0000-0002-0219-1598

Received: January 12, 2026
Accepted: May 12, 2026
Published: May 15, 2026

Cite as: Gören, İ. E. (2026). Postmortem redistribution of tetrahydrocannabinol: a data reconstruction comparison of controlled animal models and human casework. Black Sea Journal of Engineering and Science, 9(3), 1432-1443.

1. Introduction

Cannabis is among the most widely used psychoactive substances worldwide and is increasingly encountered in clinical, public health, and forensic contexts. In medicolegal investigations, cannabinoids may be detected in a wide range of scenarios, including traumatic deaths, sudden deaths, and complex polydrug intoxications, and their interpretation can influence opinions on impairment, contributory toxicity, and manner of death (Giroud et al., 2004; Delteil et al., 2018; Lemos and Ingle, 2011; Beirness et al., 2021; Rock et al., 2022). While cannabis-related mortality is multifactorial and often confounded by co-exposures and circumstances, the presence and pattern of cannabinoids in postmortem specimens frequently prompts interpretive questions, particularly when delta-9-tetrahydrocannabinol (THC) is detected at low-to-moderate concentrations or when central and peripheral results diverge (Lemos and Ingle, 2011; Rock et al., 2022).

THC is the primary psychoactive constituent of cannabis and exhibits high lipophilicity, extensive tissue distribution, and complex pharmacokinetics. In living subjects, the time course of THC and its major carboxy metabolite (THC-COOH) has been used to support estimates of recency of use, although such approaches are inherently uncertain and are not directly transferable to postmortem interpretation (Huestis et al., 2005). In postmortem toxicology, additional uncertainty arises because measured concentrations can be influenced by postmortem interval, sampling site, specimen handling, and biochemical and physical processes occurring after death (Drummer, 2008; Sastre et al., 2018; Peters and Steuer, 2019). These challenges are well recognized across drug classes and are particularly relevant for compounds prone to postmortem redistribution.

Postmortem redistribution refers to post-death changes in drug concentrations caused by diffusion from tissues into blood, decomposition-related changes, and shifts

driven by physicochemical properties and anatomical proximity to drug-rich reservoirs (Drummer, 2008; Sastre et al., 2018; Peters and Steuer, 2019). A practical way to evaluate this phenomenon is to compare central blood (commonly cardiac) with peripheral blood (commonly femoral) and express the difference as a central-to-peripheral (C/P) ratio. Although the C/P ratio is not a mechanistic measure, it is widely used as an operational indicator of site-dependent distortion and has been applied in both general postmortem redistribution frameworks and drug-specific evaluations (Drummer, 2008; Mantinieks et al., 2021; Peters and Steuer, 2019). Importantly, studies in other drugs, such as morphine, have shown that the C/P ratio can be affected by multiple variables beyond time alone, emphasizing that redistribution is not a uniform process and may differ substantially between controlled settings and heterogeneous human casework (Kamphuis et al., 2021).

For cannabinoids, the evidence base includes method-focused studies, human case series, statistical analyses of casework datasets, and controlled animal experiments. In humans, cannabinoids have been quantified in postmortem blood and tissues in multiple studies, with reports describing broad inter-individual variability and substantial dependence on sampling site and matrix (Holland et al., 2011; Gronewold and Skopp, 2011; Andrews and Paterson, 2012; Andrews et al., 2015; Saenz et al., 2017; Peters and Steuer, 2019; Hoffman et al., 2020; Cliburn et al., 2021; Meneses and Hernandez, 2021; Hansen et al., 2023).Some investigations have specifically addressed time-dependent changes in THC concentrations in deceased persons, while others have assessed distribution across matrices such as brain, muscle, and alternative specimens (Rodda et al., 2018; Chu et al., 2021; Palazzoli et al., 2021; Hansen et al., 2023; Wachholz et al., 2024). Stability considerations are also relevant because storage temperature and postmortem handling may influence measured cannabinoid concentrations in certain matrices (Santunione et al., 2023). Collectively, these reports support a cautious interpretive stance, particularly when inferring impairment or acute intoxication solely from postmortem THC concentrations (Schwerdt and Gill, 2018; Kacinko et al., 2024). Recent studies have also expanded the field through alternative-matrix evaluation, stability studies, and statistical/meta-analytic assessment of postmortem cannabinoid redistribution, indicating that interpretation depends not only on concentration values themselves but also on matrix selection, storage conditions, and analytical framing (Hansen et al., 2023; Santunione et al., 2023; Tascon et al., 2023; Wachholz et al., 2024).

A key unresolved issue in the postmortem cannabinoid literature is not whether THC redistribution can occur, but whether the magnitude and time dependence observed in controlled experimental models are transferable to heterogeneous human forensic casework. Controlled animal studies have reported pronounced and time-dependent postmortem changes in THC concentrations under standardized conditions, whereas human casework and meta-analytic evaluations suggest that central-to-peripheral (C/P) ratios in real-world settings are often closer to unity and considerably more variable (Brunet et al., 2010; Holland et al., 2011; Hoffman et al., 2020; Schaefer et al., 2020; Chu et al., 2021; Cliburn et al., 2023; Tascon et al., 2023). Although these studies have collectively advanced the field, the available evidence remains fragmented across study designs, matrices, and reporting formats. Consequently, there is still no harmonized comparative framework directly testing whether paired central and peripheral THC measurements derived from controlled animal models and routine human autopsy casework follow comparable redistribution patterns.

Accordingly, this study applied a retrospective data reconstruction and harmonization strategy to assemble paired cardiac and femoral blood measurements from controlled animal models and human forensic casework into a single analyzable dataset. The aims were to compare the distribution of THC C/P ratios between these two domains, to evaluate whether postmortem interval shows a similar relationship with C/P ratio across controlled and casework settings, and to assess whether THC-COOH provides a more stable interpretive context than parent THC (Huestis et al., 2005; Holland et al., 2011; Saenz et al., 2017; Tascon et al., 2023). The working hypothesis was that controlled animal models would show larger and more time-dependent C/P shifts than human casework, whereas THC-COOH would remain comparatively more stable across sampling sites. By structuring the study as a harmonized cross-domain comparison rather than a descriptive literature summary, the present work aims to provide a clearer analytical basis for the forensic interpretation of postmortem cannabinoid findings.

2. Materials and Methods

2.1. Study Design and Data Source

This work was designed as a retrospective, literature-based data reconstruction study focusing on postmortem cannabinoid redistribution patterns. The novel methodological contribution of this study lies in the retrospective reconstruction and harmonization of dispersed paired central and peripheral cannabinoid measurements from controlled animal experiments and heterogeneous human forensic casework into a single analyzable dataset. Compared with existing studies, this approach improves upon the literature by reducing fragmentation across study designs and by enabling direct comparison of paired central and peripheral cannabinoid measurements under a common analytical structure. This allowed assessment of cross-domain consistency in THC redistribution patterns between controlled animal models and human autopsy casework, which is difficult to achieve when studies are interpreted

individually. This design enabled direct cross-domain comparison of THC redistribution patterns under a common analytical framework, which is not usually possible when these data remain isolated within individual experimental or case-based reports. This approach was intended to permit direct cross-domain comparison under a common analytical structure, rather than relying on isolated descriptive interpretation of individual studies. The objective was to quantify site-dependent differences using paired cardiac and femoral blood measurements within the broader postmortem redistribution framework (Drummer, 2008; Peters and Steuer, 2019; Sastre et al., 2018). In this respect, the methodological contribution of the study is not the generation of new primary measurements, but the creation of a structured comparative framework for evaluating redistribution behaviour across otherwise non-comparable sources.

2.2. Systematic Literature Search

A structured literature search was conducted in PubMed, Scopus, and Web of Science, covering publications from January 1, 1990 to December 31, 2024. The search strategy was designed to identify studies reporting postmortem cannabinoid concentrations in matrices relevant to redistribution analysis. Core search terms included postmortem, THC, tetrahydrocannabinol, cannabinoids, postmortem redistribution, cardiac blood, femoral blood, porcine, and rabbit, with syntax adapted to each database. The search results were screened first at the title and abstract level, and full texts were assessed when eligibility could not be determined from the initial record. In total, 52 potentially relevant records were identified for assessment, and the studies meeting the predefined eligibility criteria were taken forward for reconstruction and harmonization.

2.3. Eligibility Criteria and Study Selection

To reduce heterogeneity and ensure that pooled estimates reflected comparable sampling concepts, eligibility was restricted to studies reporting quantitative cannabinoid concentrations in postmortem specimens, with emphasis on paired central–peripheral sampling that enables calculation of a central-to-peripheral ratio (Gronewold and Skopp, 2011; Holland et al., 2011; Kemp et al., 2015; Lemos and Ingle, 2011). Studies were considered eligible when they provided numerical THC and/or metabolite concentrations (THC-COOH and/or 11-OH-THC) in postmortem matrices, and paired cardiac (central) and femoral (peripheral) blood data at the individual-case level or in a form that could be reconstructed. Controlled animal studies were eligible when dose administration and postmortem conditions were described sufficiently to interpret time-dependent changes under standardized conditions (Brunet et al., 2010; Cliburn et al., 2023; Schaefer et al., 2020). Autopsy series were eligible when postmortem interval (PMI) and sampling sites were documented in a manner allowing paired comparisons (Chu et al., 2021; Holland et al., 2011; Kemp et al., 2015; Lemos and Ingle, 2011).

Records were excluded if they reported only qualitative findings (presence/absence), lacked central–peripheral pairing, focused on synthetic cannabinoids without THC data (Gaunitz et al., 2018), or addressed cannabinoid effects without a postmortem distribution/PMR component (e.g., mechanistic work centered on mitochondrial outcomes rather than postmortem toxicological interpretation) (Charles et al., 2024; Quenardelle et al., 2025). To improve comparability across sources, inclusion was restricted to studies providing extractable paired central and peripheral measurements or sufficient quantitative information for reconstruction at the individual-case level. This restriction was applied to reduce conceptual heterogeneity and to ensure that the final pooled dataset reflected comparable sampling logic across studies. Following selection, 32 studies formed the quantitative evidence base described in Supplementary Tables S1 and S2. Studies not contributing extractable quantitative pairing were retained only to contextualize interpretation and known pitfalls in the Discussion (Kacinko et al., 2024; Schwerdt and Gill, 2018; Tascon et al., 2023). Study-level characteristics of all quantitatively included sources are summarized in Supplementary Table S1.

2.4. Data Extraction and In Silico Reconstruction

Data were extracted into a standardized electronic form at both the study level and the case level. Study-level information included study identifier, first author, publication year, species, group type, number of cases, matrix analyzed, and the principal qualitative finding, as summarized in Supplementary Table S1. Case-level reconstruction included cohort, species, reference source, postmortem interval (PMI, hours), body position when available, femoral THC concentration, cardiac THC concentration, calculated central-to-peripheral (C/P) ratio, and paired femoral and cardiac THC-COOH values when reported, as summarized in Supplementary Table S2.

When individual paired values were reported in tables or text, the data were directly transcribed. When quantitative values were presented only in graphical form, figure-based digitization was performed using WebPlotDigitizer (version 4.6). In such cases, plot axes were calibrated before point extraction, and the reconstructed values were then transferred into the standardized dataset. This approach was used only when the graphical presentation contained extractable quantitative information and is consistent with accepted secondary reconstruction approaches when raw numerical tables are not available (Guyot et al., 2012).

To improve consistency across studies, concentrations were harmonized into ng/mL for blood-based matrices, paired observations were linked to their original source study, and each reconstructed observation was assigned a unique case identifier. The final reconstructed dataset comprised 948 paired observations and formed the basis of the comparative analyses presented in this study

(Supplementary Table S2).

2.5. Potential Sources of Bias and Methodological Limitations

As this study was based on retrospective reconstruction from published sources, several potential sources of bias were considered. First, the included studies differed in analytical method, case composition, sampling conditions, and postmortem context. Second, some quantitative values were reconstructed from figures rather than extracted directly from numeric tables, which may introduce limited measurement uncertainty. Third, key contextual variables such as storage conditions, body position, agonal state, and pre-analytical handling were not uniformly reported across all studies. To reduce these effects, inclusion was restricted to studies with paired central and peripheral data or reconstructable quantitative equivalents, concentrations were harmonized to a common unit where applicable, and all analyses were interpreted as comparative rather than causal estimates. These limitations were also taken into account in the interpretation of the findings.

2.6. Cohort Definition

To contrast controlled redistribution behavior against real-world forensic variability, data were grouped into two principal cohorts:

1) Controlled animal models (n = 59; porcine n = 27 and rabbit n = 32), representing experimentally defined dosing and postmortem conditions (Brunet et al., 2010; Cliburn et al., 2023; Schaefer et al., 2020).
2) Human postmortem casework (n = 889), representing routine autopsy toxicology with heterogeneous PMI and case circumstances (Chu et al., 2021; Holland et al., 2011; Kemp et al., 2015; Lemos and Ingle, 2011; Tascon et al., 2023).

2.7. Outcome Definitions and Statistical Analysis

The primary indicator of redistribution was the central-to-peripheral ratio (C/P ratio), calculated for THC as (equation 1):

$$\text{C/P ratio} = \frac{[\text{THC}]_{\text{cardiac blood}}}{[\text{THC}]_{\text{femoral blood}}} \quad (1)$$

An analogous ratio was also computed for THC-COOH when paired values were available, to provide metabolite context in line with prior cannabinoid distribution literature (Holland et al., 2011; Saenz et al., 2017; Tascon et al., 2023). Normality was assessed using the Shapiro–Wilk test. Because C/P ratios were non-normally distributed, cohort comparisons were performed using the Mann–Whitney U test. Associations between PMI and C/P ratio were evaluated using Spearman rank correlation (ρ). Statistical significance was set at $p < 0.05$. Analyses were conducted on the reconstructed dataset summarized in Supplementary Table S2.

In addition to the primary comparative analyses, an exploratory predictive modeling framework was applied to evaluate whether femoral THC concentrations could be estimated from reconstructed case-level variables. Two modeling approaches, linear regression and Random Forest regression, were used in order to compare a conventional parametric model with a non-linear ensemble-based approach. Model performance was assessed separately in the animal and human cohorts using the coefficient of determination (R^2) and root mean square error (RMSE). This component was included to test whether THC redistribution patterns derived from controlled experimental conditions were more analytically predictable than those observed in heterogeneous forensic casework.

3. Results

3.1. Magnitude of Redistribution

The reconstructed dataset comprised 948 paired observations, including controlled animal models (n = 59) and human casework (n = 889). THC central-to-peripheral (C/P) ratios differed between the two cohorts (Figure 1; Table 1).

Table 1. Comparative statistics of THC central-to-peripheral (C/P) ratios in controlled animal models and human postmortem casework

Variable	Cohort I: Animal Models (n=59)	Cohort II: Human Casework (n=889)	P-value
Study design	Controlled (fixed conditions)	Retrospective (variable conditions)	–
Typical PMI window	< 6 h	12–72 h	<0.001*
THC C/P ratio			
Mean ± SD	2.85 ± 0.64	1.12 ± 0.41	<0.001*
Median	2.78	1.04	–
Range	1.4–4.1	0.3–5.2	–
Reverse distribution (C/P < 1.0)	0%	38.4%	–
PMI vs C/P correlation (Spearman ρ)	0.93	−0.11	–

* Mann–Whitney U test; significance threshold $p < 0.05$. Animal models include porcine and rabbit datasets reconstructed from the literature, whereas the human cohort includes reconstructed autopsy casework. C/P ratio was calculated as cardiac blood THC concentration divided by femoral blood THC concentration. "Reverse distribution" denotes paired observations with C/P < 1.0. PMI = postmortem interval; SD = standard deviation; ρ = Spearman correlation coefficient. p values are shown where statistical comparison was performed. *Mann–Whitney U test; significance threshold $p < 0.05$.

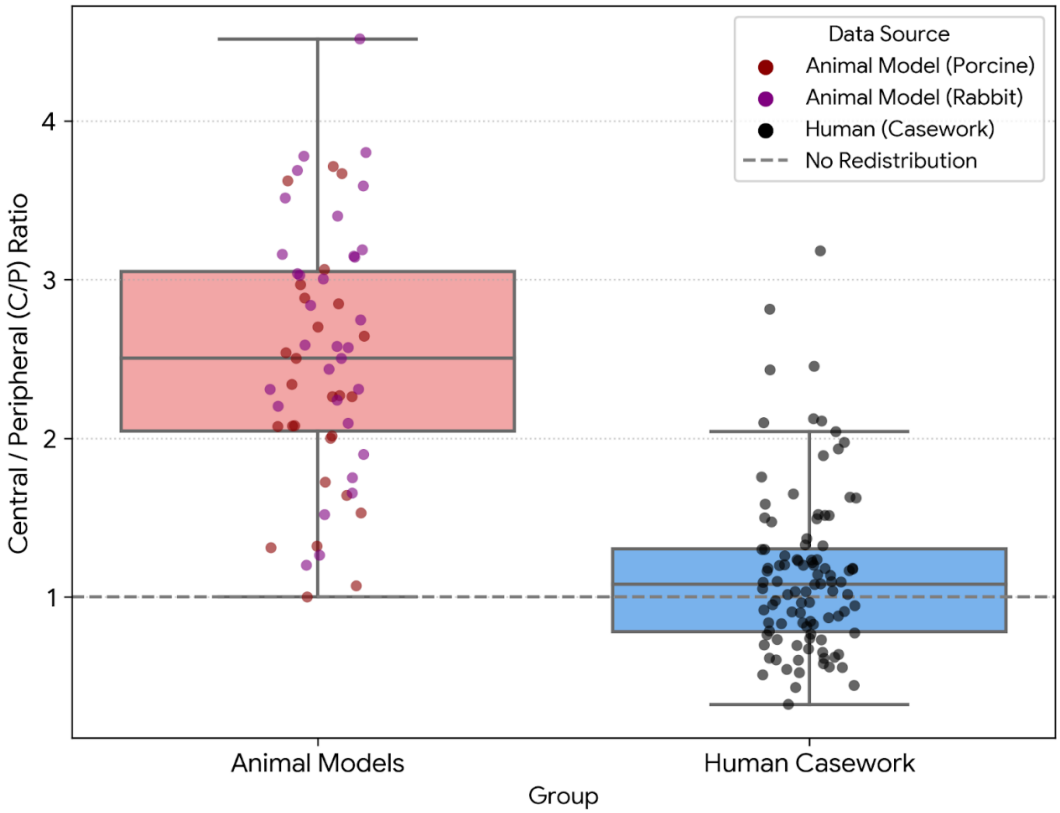

Figure 1. Distribution of THC central-to-peripheral (C/P) ratios in controlled animal models and human casework. Boxplots summarize the overall animal and human cohorts, while individual points represent reconstructed observations from porcine studies, rabbit studies, and human autopsy casework. The dashed horizontal line at C/P = 1.0 indicates equality between cardiac and femoral THC concentrations.

The median C/P ratio was 2.78 in animal models and 1.04 in human casework. Mean (±SD) values were 2.85 ± 0.64 for animals and 1.12 ± 0.41 for humans. The between-cohort difference was statistically significant (Mann–Whitney U, $p < 0.001$). In human casework, 38.4% of observations showed C/P < 1.0, whereas no C/P < 1.0 values were observed in the animal datasets (Table 1).

3.2. Relationship Between PMI and C/P Ratio

The relationship between postmortem interval (PMI) and THC C/P ratio differed between cohorts (Figure 2; Table 1). In controlled animal models, PMI showed a strong positive association with C/P ratio (Spearman $\rho = 0.93$). In human casework, no meaningful monotonic association was observed (Spearman $\rho = -0.11$). Human observations were distributed across a wider PMI range and showed broader dispersion in C/P ratios than the animal cohort (Figure 2).

3.3. Cross-Matrix THC Concentration Patterns

A subset of reconstructed data including blood, tissue, and alternative matrices was evaluated to compare THC concentration levels across matrices (Table 2; Figure 3). Mean THC concentrations were 766.0 in lung tissue, 759.3 in heart blood, 92.4 in liver tissue, 15.6 in femoral blood, and 14.8 in intraosseous fluid (IOF). Relative to femoral blood, lung tissue and heart blood were higher by 49.1-fold and 48.7-fold, respectively, whereas liver tissue was 5.9-fold higher and IOF was 0.95-fold relative to femoral blood (Table 2).

3.4. Predictive Modelling

Prediction of femoral THC concentration from reconstructed variables showed different performance across cohorts (Table 3; Figure 4). In the animal cohort, linear regression yielded $R^2 = 0.91$ and RMSE = 3.5, while Random Forest regression yielded $R^2 = 0.93$ and RMSE = 3.0. In human casework, linear regression yielded $R^2 = 0.38$ and RMSE = 6.2, while Random Forest regression yielded $R^2 = 0.39$ and RMSE = 6.0. Predicted versus observed values showed closer agreement in the animal cohort than in the human cohort (Figure 4).

3.5. Metabolite Patterning: THC Versus THC-COOH and Ratio Distortion

When paired metabolite data were available, THC-COOH showed a mean C/P ratio of approximately 1.05, whereas parent THC showed higher C/P ratios in the summarized dataset (Table 4). In the paired concentration comparison shown in Figure 5, femoral concentrations were 15.6 ng/mL for THC and 45.0 ng/mL for THC-COOH, whereas cardiac concentrations were 60.5 ng/mL and 47.0 ng/mL, respectively. The cardiac–femoral difference was therefore greater for THC than for THC-COOH (Figure 5; Table 4).

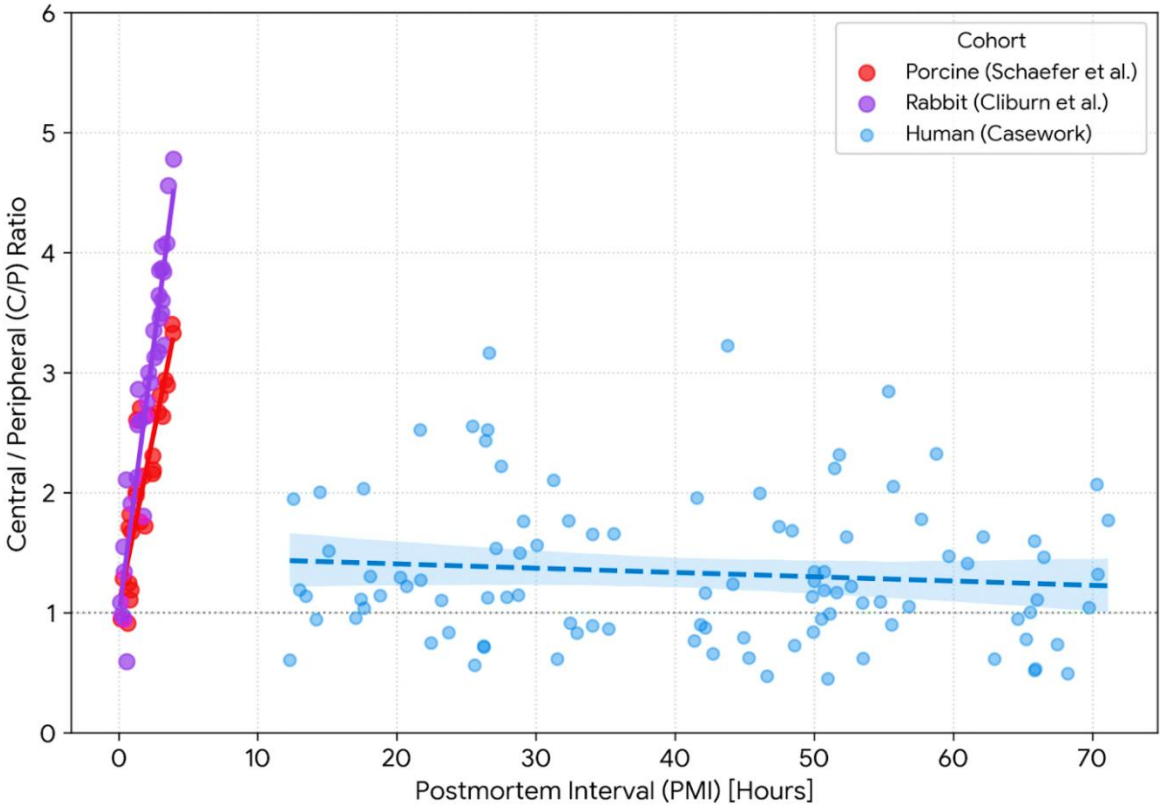

Figure 2. Relationship between postmortem interval (PMI) and THC central-to-peripheral (C/P) ratio in reconstructed porcine, rabbit, and human casework observations. Each point represents a paired observation, and the plotted lines indicate cohort-specific trends across PMI values. The dashed horizontal line at C/P = 1.0 indicates equality between cardiac and femoral THC concentrations. PMI = postmortem interval.

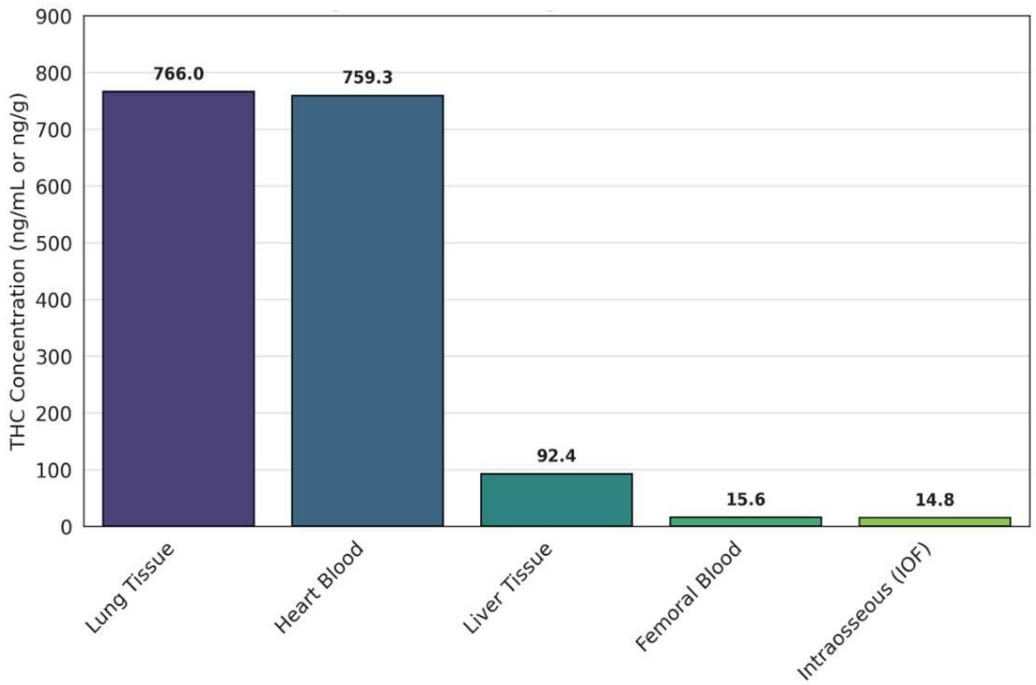

Figure 3. Cross-matrix THC concentration levels in the reconstructed dataset. Bars represent mean THC concentrations across lung tissue, heart blood, liver tissue, femoral blood, and intraosseous fluid (IOF) in the reconstructed cross-matrix subset. Tissue concentrations are expressed as ng/g, whereas fluid concentrations are expressed as ng/mL. Numeric labels above the bars indicate the corresponding mean values.

Table 2. Mean THC concentrations across tissue, blood, and alternative matrices in the reconstructed cross-matrix subset*

Matrix / Tissue	Mean THC conc.	Fold vs femoral blood
Lung tissue	766.0 ng/g	49.1×
Heart blood (central)	759.3 ng/mL	48.7×
Liver tissue	92.4 ng/g	5.9×
Femoral blood (peripheral)	15.6 ng/mL	1.0×
Intraosseous fluid (IOF)	14.8 ng/mL	0.95×

* Fold values are expressed relative to femoral blood, which was used as the reference matrix (1.0×). Concentrations are reported as ng/mL for blood and intraosseous fluid and as ng/g for tissue matrices. IOF = intraosseous fluid.

Table 3. Predictive performance of linear regression and Random Forest models for estimating femoral THC concentration from reconstructed case-level variables in animal models and human casework*

Cohort	Linear Regression (R^2; RMSE)	Random Forest (R^2; RMSE)
Animal models	0.91; 3.5	0.93; 3.0
Human casework	0.38; 6.2	0.39; 6.0

*Model performance is summarized using the coefficient of determination (R^2) and root mean square error (RMSE). Higher R^2 and lower RMSE indicate better predictive agreement. Values are reported separately for the animal and human cohorts.

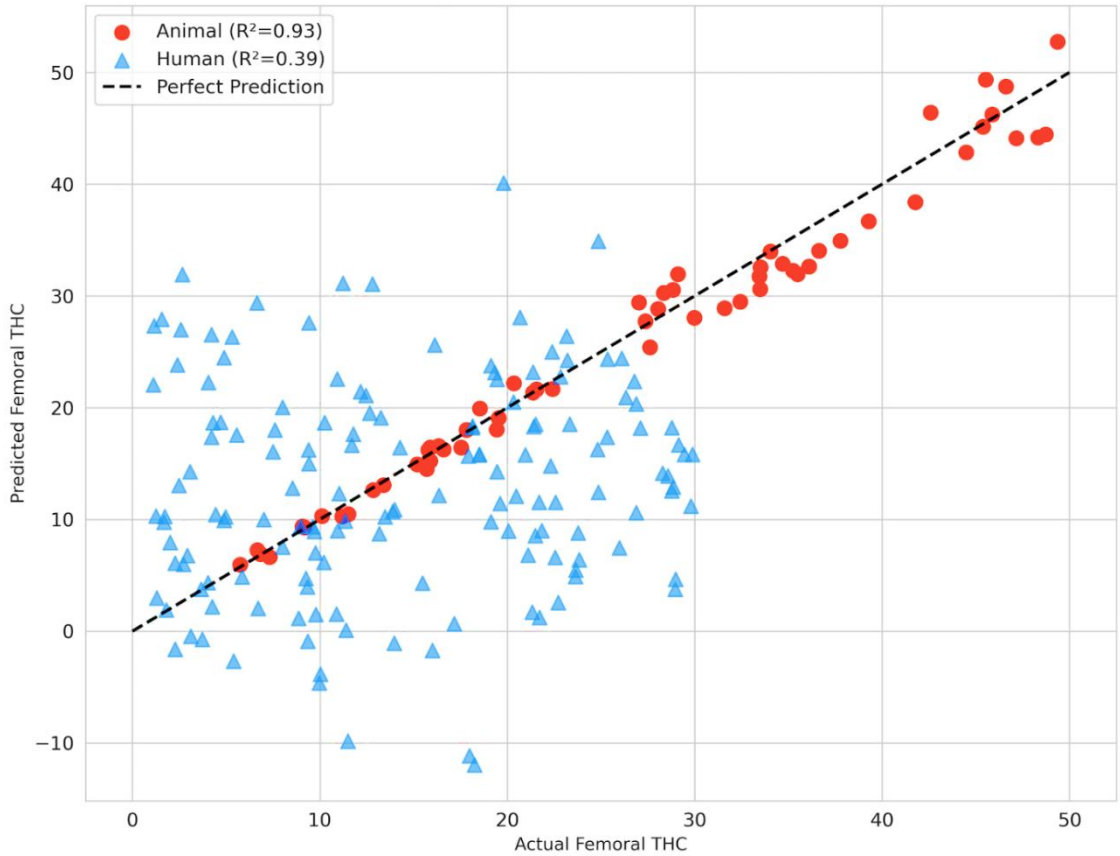

Figure 4. Predicted versus observed femoral THC concentrations in animal and human cohorts for the Random Forest model. Each point represents a reconstructed observation. Red circles denote the animal cohort and blue triangles denote the human cohort. The dashed diagonal line represents perfect agreement between observed and predicted values (y = x). R^2 = coefficient of determination.

Table 4. Paired femoral and cardiac concentrations and central-to-peripheral ratios of THC and THC-COOH in the reconstructed paired dataset*

Analyte	Femoral concentration (ng/mL)	Cardiac concentration (ng/mL)	Cardiac–femoral difference	C/P ratio
THC	15.6	60.5	+44.9	3.88
THC-COOH	45.0	47.0	+2.0	1.04

*Cardiac–femoral difference was calculated as cardiac concentration minus femoral concentration. C/P ratio was calculated as cardiac concentration divided by femoral concentration. THC = delta-9-tetrahydrocannabinol; THC-COOH = 11-nor-9-carboxy-delta-9-tetrahydrocannabinol.

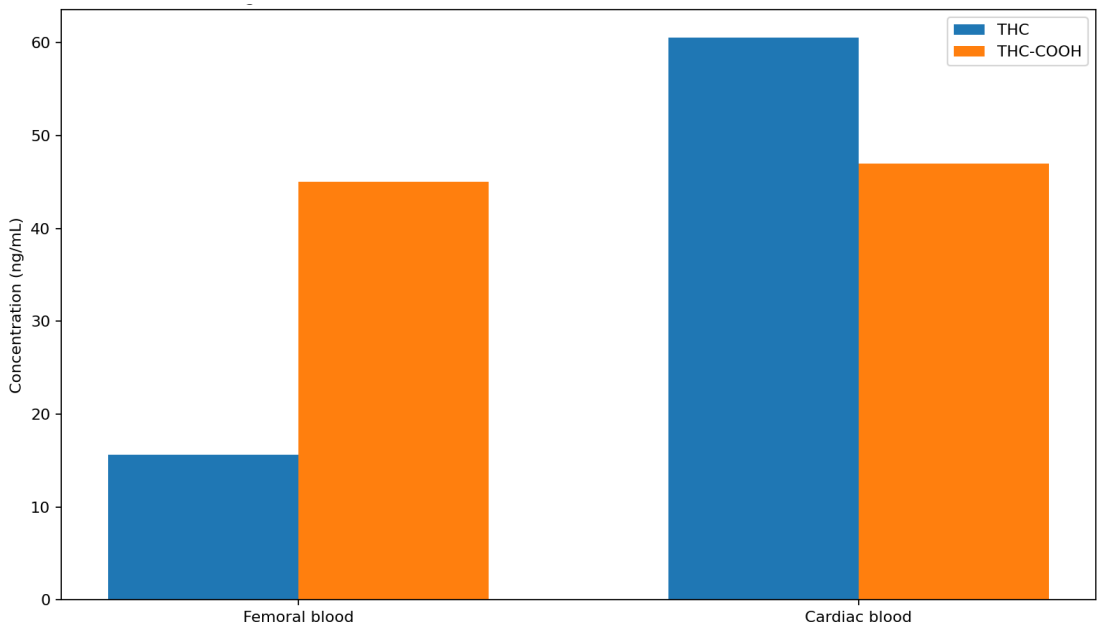

Figure 5. Paired femoral and cardiac concentrations of THC and THC-COOH in the reconstructed dataset. Bars show summarized concentrations in femoral and cardiac blood for parent THC and the major metabolite THC-COOH. Concentrations are expressed as ng/mL. THC = delta-9-tetrahydrocannabinol; THC-COOH = 11-nor-9-carboxy-delta-9-tetrahydrocannabinol.

4. Discussion

This reconstructed dataset demonstrates a consistent and practically important divergence between controlled animal models and human postmortem casework in how THC distributes between central and peripheral blood. In controlled porcine and rabbit studies, THC C/P ratios were uniformly above 1.0 and increased with PMI, whereas human casework clustered close to unity and frequently showed C/P values below 1.0. This contrast aligns with earlier human observations of wide cannabinoid variability across matrices and cases (Gronewold and Skopp, 2011; Hoffman et al., 2020; Holland et al., 2011; Tascon et al., 2023) and with the general PMR literature emphasizing that central blood is more vulnerable to postmortem artifacts than peripheral blood (Drummer, 2008; Peters and Steuer, 2019; Sastre et al., 2018). The implication is methodological rather than philosophical: interpretations built primarily on controlled early postmortem animal kinetics may overestimate the magnitude and predictability of THC redistribution in routine medicolegal settings. This interpretation is supported not only by the difference in central tendency between cohorts, but also by the difference in distributional structure. In particular, the absence of C/P < 1.0 values in the animal cohort and their substantial prevalence in human casework indicate that the two cohorts do not reflect the same redistribution pattern with different magnitudes, but rather distinct analytical domains with different levels of variability. In this respect, the scientific contribution of the present study lies in demonstrating, within a single harmonized reconstructed dataset, that THC redistribution patterns observed in controlled animal models and those observed in human postmortem casework differ not only in magnitude but also in analytical structure. By integrating paired central and peripheral measurements across otherwise separate evidence domains, the study provides a comparative framework for evaluating the transferability of experimental redistribution patterns to routine forensic interpretation.

The strong PMI–C/P correlation in animals is consistent with designs that intentionally capture the early postmortem window under standardized position and temperature, where concentration gradients are still forming and diffusion is likely to be time-sensitive (Brunet et al., 2010; Cliburn et al., 2023; Schaefer et al.,

2020). In contrast, human autopsy series often involve longer and more heterogeneous PMI ranges, variable storage and ambient conditions, and unmeasured pre-analytical factors that can mask any monotonic time dependence (Peters and Steuer, 2019; Sastre et al., 2018). Human data on time-dependent changes in THC also suggest that patterns are not uniform across cases and may depend on contextual variables that are rarely captured systematically in routine toxicology reporting (Chu et al., 2021; Tascon et al., 2023). From an analytical perspective, this contrast is important because PMI explained a substantial portion of the variation in C/P ratio in the controlled cohort ($\rho = 0.93$) but contributed little explanatory value in the human cohort ($\rho = -0.11$). Therefore, PMI alone, particularly within typical autopsy timeframes, should not be assumed to provide a reliable correction factor for central-to-peripheral THC differences in routine casework.

The cross-matrix gradients in the reconstructed tissue subset support a plausible anatomical explanation for elevated cardiac THC: central blood can be influenced by nearby, THC-rich compartments. Experimental work has shown that postmortem concentration changes of THC can occur in pigs under controlled conditions (Brunet et al., 2010; Schaefer et al., 2020), and similar time- and temperature-dependent behaviour has been demonstrated in rabbits after controlled inhalation (Cliburn et al., 2023). These findings are compatible with a proximity-driven mechanism in which diffusion from adjacent tissues contributes disproportionately to central blood. This is consistent with broader PMR principles, where drugs can move from organs and tissues into central vasculature after death, and where sampling site is a major determinant of measured concentration (Drummer, 2008; Peters and Steuer, 2019; Sastre et al., 2018). This interpretation is supported by the marked quantitative separation observed in the reconstructed subset, where lung tissue and heart blood showed approximately 49-fold and 48-fold higher THC concentrations than femoral blood, whereas intraosseous fluid remained close to femoral levels. Importantly, the present results do not require a single universal "reservoir" in every case; rather, they emphasize that central blood THC may be a composite signal reflecting both systemic circulation and local postmortem influence, whereas femoral blood is more likely to approximate a peripheral compartment less affected by local diffusion.

A substantial fraction of human observations showed femoral concentrations equal to or exceeding cardiac concentrations. Such patterns are not incompatible with PMR theory; instead, they highlight that casework data reflect a mixture of processes sampling variability, postmortem handling, and biological heterogeneity rather than a single-direction kinetic process. The PMR literature has repeatedly underscored that central/peripheral comparisons can be influenced by multiple variables beyond time, including body position, temperature, resuscitation, cause of death, and sampling technique (Drummer, 2008; Peters and Steuer, 2019; Sastre et al., 2018). In addition, cannabinoids are frequently interpreted in contexts where per se thresholds or simplistic rules can be misleading, particularly when postmortem artifacts and chronic use patterns coexist (Kacinko et al., 2024; Schwerdt and Gill, 2018). The observed prevalence of $C/P < 1.0$ in 38.4% of human observations supports an interpretive approach that treats cardiac THC as a higher-variance matrix and avoids over-weighting it in isolation.

Across available paired data, THC-COOH exhibited central-to-peripheral ratios near unity compared with parent THC, consistent with prior postmortem cannabinoid distribution studies that emphasize metabolite patterns and matrix selection for interpretation (Holland et al., 2011; Saenz et al., 2017; Tascon et al., 2023). In the summarized paired comparison, the cardiac–femoral difference was 44.9 ng/mL for THC but only 2.0 ng/mL for THC-COOH, further supporting the quantitative separation between parent and metabolite behaviour. This divergence is forensically relevant because ratios involving parent THC may be inflated in central blood when parent THC is susceptible to site-dependent distortion, while THC-COOH remains comparatively stable. The practical takeaway is that femoral blood and metabolite-aware interpretation (including THC-COOH) are likely to yield more defensible conclusions than relying on cardiac THC alone, especially when the question involves recency or "acute" exposure narratives (Huestis et al., 2005; Schwerdt and Gill, 2018).

The predictive modelling component reinforces the same message from a different angle. Models trained on controlled animal data performed well, while performance fell markedly in humans despite using non-linear algorithms. This pattern is most parsimoniously interpreted as a domain shift: animal datasets reflect controlled conditions with fewer unmeasured drivers, whereas human casework contains latent variables that dominate variance but are not represented in the feature set (Drummer, 2008; Peters and Steuer, 2019). The modelling exercise is therefore best viewed as evidence that femoral THC cannot be reliably inferred from cardiac THC and PMI alone in real casework. Analytically, this interpretation is supported by the marked decline in model performance from the controlled cohort (R^2 = 0.91–0.93) to the human cohort (R^2 = 0.38–0.39), together with the minimal improvement achieved by the non-linear model in human data. This pattern suggests that important sources of variation in human postmortem THC distribution are not captured by the reconstructed variables alone, rather than simply reflecting insufficient model complexity.

Several limitations should be considered in interpreting the present findings. First, the reconstructed dataset was derived from heterogeneous published studies that differed in analytical methods, case composition,

postmortem conditions, and reporting quality; therefore, the observed cohort-level differences should not be interpreted as if they originated from a single standardized design. Second, the animal and human datasets differed not only in biological context, but also in sample size, PMI range, and degree of pre-analytical control, which may have contributed to the contrast observed between the two domains. Third, some quantitative values were reconstructed from figures rather than extracted directly from numerical tables, introducing an additional source of measurement uncertainty despite the use of established digitization procedures. In addition, several potentially relevant variables, including body position, storage conditions, agonal interval, resuscitation history, and sampling conditions, were not consistently reported across studies and therefore could not be incorporated systematically into the analyses. The predictive modelling results should also be interpreted cautiously, as they were exploratory and based only on variables available in the reconstructed dataset, rather than developed as validated forensic prediction tools. Finally, publication and reporting bias cannot be excluded. These limitations do not negate the overall cross-domain pattern observed in the study, but they do limit mechanistic inference and argue against translating the pooled findings into rigid quantitative thresholds for individual case interpretation. Taken together, the results provide a comparative basis for a more cautious forensic interpretation of postmortem THC findings, particularly when observations from controlled experimental models are considered alongside heterogeneous human casework. Accordingly, peripheral blood should be prioritized for quantitative assessment, cardiac THC should be interpreted as a more variable matrix susceptible to postmortem artifacts, and THC-COOH should be incorporated to contextualize parent THC findings (Holland et al., 2011; Saenz et al., 2017; Tascon et al., 2023). Where available, alternative matrices that approximate peripheral behaviour may further reduce interpretive uncertainty (Hansen et al., 2023; Rodda et al., 2018; Zughaibi et al., 2023). This interpretation is also consistent with recent work incorporating alternative matrices, storage-related stability assessment, and statistical/meta-analytic evaluation, all of which suggest that postmortem cannabinoid interpretation requires integration of toxicological, analytical, and matrix-dependent perspectives rather than reliance on a single concentration measure (Hansen et al., 2023; Santunione et al., 2023; Tascon et al., 2023; Wachholz et al., 2024). These points align with broader cautions in the forensic literature regarding reliance on single-matrix, single-analyte postmortem cannabinoid results for conclusions about impairment or acute intoxication (Kacinko et al., 2024; Schwerdt and Gill, 2018).

5. Conclusion

This retrospective data reconstruction study, based on 948 paired observations extracted from quantitative postmortem cannabinoid literature, demonstrates a pronounced divergence between controlled animal models and human forensic casework in the postmortem behaviour of THC. Controlled porcine and rabbit studies showed consistently elevated and time-dependent central-to-peripheral ratios, whereas human casework clustered near unity and frequently exhibited ratios below 1.0, indicating that redistribution patterns observed under standardized experimental conditions do not generalize reliably to routine autopsy settings. Across available paired data, THC-COOH remained comparatively stable between cardiac and femoral compartments, supporting its value as contextual information when interpreting parent THC in postmortem specimens. Collectively, these findings reinforce that femoral blood should be prioritized for quantitative interpretation, and that cardiac THC results should be treated as a higher-variance matrix susceptible to site-dependent distortion. The presented pooled dataset and reconstruction approach provide an evidence-based basis for more cautious and defensible interpretation of postmortem cannabinoid findings, particularly when case narratives involve recency of use or acute exposure.

Author Contributions

The percentages of the author' contributions are presented below. The author reviewed and approved the final version of the manuscript.

	İ.E.G.
C	100
D	100
S	100
DCP	100
DAI	100
L	100
W	100
CR	100
SR	100
PM	100
FA	100

C= concept, D= design, S= supervision, DCP= data collection and/or processing, DAI= data analysis and/or interpretation, L= literature search, W= writing, CR= critical review, SR= submission and revision, PM= project management, FA= funding acquisition.

Conflict of Interest

The author declared that there is no conflict of interest.

Ethical Consideration

Ethics committee approval was not required for this

study because of there was no study on animals or humans.

References

Andrews, R., & Paterson, S. (2012). A validated method for the analysis of cannabinoids in post-mortem blood using liquid–liquid extraction and two-dimensional gas chromatography–mass spectrometry. *Forensic Science International*, *222*(1–3), 111–117. https://doi.org/10.1016/j.forsciint.2012.05.007

Andrews, R., Murphy, K. G., Nahar, L., & Paterson, S. (2015). Cannabinoid concentrations detected in fatal road traffic collision victims compared with a population of other postmortem cases. *Clinical Chemistry*, *61*(10), 1256–1264. https://doi.org/10.1373/clinchem.2015.240846

Beirness, D. J., Gu, K. W., Lowe, N. J., Woodall, K. L., Desrosiers, N. A., Cahill, B., Porath, A. J., & Peaire, A. (2021). Cannabis, alcohol and other drug findings in fatally injured drivers in Ontario. *Traffic Injury Prevention*, *22*(1), 1–6. https://doi.org/10.1080/15389588.2020.1847281

Brunet, B., Hauet, T., Hébrard, W., Papet, Y., Mauco, G., & Mura, P. (2010). Postmortem redistribution of THC in the pig. *International Journal of Legal Medicine*, *124*(6), 543–549. https://doi.org/10.1007/s00414-009-0403-2

Charles, A.-L., Giannini, M., Meyer, A., Charloux, A., Talha, S., Vogel, T., Raul, J.-S., Wolff, V., & Geny, B. (2024). Cannabis (THC) aggravates the deleterious effects of alcohol (EtOH) on skeletal muscles' mitochondrial respiration: Modulation by age and metabolic phenotypes. *Biology*, *13*(12), Article 1080. https://doi.org/10.3390/biology13121080

Chu, M., Rago, M. Di, Mantinieks, D., Glowacki, L., Woodford, N. W., Gerostamoulos, D., & Drummer, O. H. (2021). Time-dependent changes in THC concentrations in deceased persons. *Journal of Analytical Toxicology*, *45*(1), 1–7. https://doi.org/10.1093/jat/bkaa052

Cliburn, K. D., Huestis, M. A., Wagner, J. R., & Kemp, P. M. (2021). Cannabinoid distribution in fatally-injured pilots' postmortem fluids and tissues. *Forensic Science International*, *329*, Article 111075. https://doi.org/10.1016/j.forsciint.2021.111075

Cliburn, K. D., Kemp, P. M., Huestis, M. A., Wagner, J. R., Payton, M., Liu, L., Liang, Y., & Maxwell, L. K. (2023). Time- and temperature-dependent postmortem Δ9-tetrahydrocannabinol concentration changes in rabbits following controlled inhaled cannabis administration. *Journal of Analytical Toxicology*, *47*(9), 850–857. https://doi.org/10.1093/jat/bkad076

Delteil, C., Sastre, C., Piercecchi, M.-D., Faget-Agius, C., Deveaux, M., Kintz, P., Devooght, M.-A., Leonetti, G., Bartoli, C., & Pélissier-Alicot, A.-L. (2018). Death by self-mutilation after oral cannabis consumption. *Legal Medicine*, *30*, 5–9. [suspicious link removed]

Drummer, O. H. (2008). Postmortem toxicological redistribution. In *Essentials of autopsy practice* (ss. 1–21). Springer. https://doi.org/10.1007/978-1-84628-835-7_1

Gaunitz, F., Lehmann, S., Thomas, A., Thevis, M., Rothschild, M. A., & Mercer-Chalmers-Bender, K. (2018). Post-mortem distribution of the synthetic cannabinoid MDMB-CHMICA and its metabolites in a case of combined drug intoxication. *International Journal of Legal Medicine*, *132*(6), 1645–1657. https://doi.org/10.1007/s00414-018-1911-8

Giroud, C., Michaud, K., Sporkert, F., Eap, C., Augsburger, M., Cardinal, P., & Mangin, P. (2004). A fatal overdose of cocaine associated with coingestion of marijuana, buprenorphine, and fluoxetine: Body fluid and tissue distribution of cocaine and its metabolites determined by hydrophilic interaction chromatography-mass spectrometry (HILIC-MS). *Journal of Analytical Toxicology*, *28*(6), 464–474. https://doi.org/10.1093/jat/28.6.464

Gronewold, A., & Skopp, G. (2011). A preliminary investigation on the distribution of cannabinoids in man. *Forensic Science International*, *210*(1–3), e7–e11. https://doi.org/10.1016/j.forsciint.2011.04.010

Guyot, P., Ades, A., Ouwens, M. J. N. M., & Welton, N. J. (2012). Enhanced secondary analysis of survival data: Reconstructing the data from published Kaplan-Meier survival curves. *BMC Medical Research Methodology*, *12*(1), Article 9. https://doi.org/10.1186/1471-2288-12-9

Hansen, S. L., Nielsen, M. K. K., Linnet, K., & Rasmussen, B. S. (2023). Suitability of cardiac blood, brain tissue, and muscle tissue as alternative matrices for toxicological evaluation in postmortem cases. *Drug Testing and Analysis*, *15*(5), 529–538. https://doi.org/10.1002/dta.3439

Hoffman, M. A., Trochta, A., Gary, R. D., Fitzgerald, R. L., & McIntyre, I. M. (2020). An evaluation of postmortem concentrations of Δ9-tetrahydrocannabinol (THC) and 11-nor-9-carboxy-Δ9-tetrahydrocannabinol (THCCOOH). *Forensic Science International*, *315*, Article 110414. https://doi.org/10.1016/j.forsciint.2020.110414

Holland, M. G., Schwope, D. M., Stoppacher, R., Gillen, S. B., & Huestis, M. A. (2011). Postmortem redistribution of Δ9-tetrahydrocannabinol (THC), 11-hydroxy-THC (11-OH-THC), and 11-nor-9-carboxy-THC (THCCOOH). *Forensic Science International*, *212*(1–3), 247–251. https://doi.org/10.1016/j.forsciint.2011.06.028

Huestis, M. A., Barnes, A., & Smith, M. L. (2005). Estimating the time of last cannabis use from plasma Δ9-tetrahydrocannabinol and 11-nor-9-carboxy-Δ9-tetrahydrocannabinol concentrations. *Clinical Chemistry*, *51*(12), 2289–2295. https://doi.org/10.1373/clinchem.2005.056838

Kacinko, S. L., Isenschmid, D. S., & Logan, B. K. (2024). Are postmortem cannabinoid concentrations forensically reliable? *American Journal of Forensic Medicine & Pathology*, *45*(1), 92–93. https://doi.org/10.1097/PAF.0000000000000887

Kamphuis, A. E. M., Borra, L. C. P., van der Hulst, R., Kloos, D.-P., Rijken, D. J., Bosman, I. J., & Touw, D. J. (2021). Postmortem redistribution of morphine in humans: Important variables that might be influencing the central blood/peripheral blood ratio. *Forensic Science International*, *329*, Article 111094. https://doi.org/10.1016/j.forsciint.2021.111094

Kemp, P. M., Cardona, P. S., Chaturvedi, A. K., & Soper, J. W. (2015). Distribution of Δ9-tetrahydrocannabinol and 11-nor-9-carboxy-Δ9-tetrahydrocannabinol acid in postmortem biological fluids and tissues from pilots fatally injured in aviation accidents. *Journal of Forensic Sciences*, *60*(4), 942–949. https://doi.org/10.1111/1556-4029.12751

Lemos, N. P., & Ingle, E. A. (2011). Cannabinoids in postmortem toxicology. *Journal of Analytical Toxicology*, *35*(7), 394–401. https://doi.org/10.1093/anatox/35.7.394

Mantinieks, D., Gerostamoulos, D., Glowacki, L., Di Rago, M., Schumann, J., Woodford, N. W., & Drummer, O. H. (2021). Postmortem drug redistribution: A compilation of postmortem/antemortem drug concentration ratios. *Journal of Analytical Toxicology*, *45*(4), 368–377. https://doi.org/10.1093/jat/bkaa107

Meneses, V., & Hernandez, M. (2021). Cannabinoid distribution in postmortem samples. *Forensic Chemistry*, *23*, Article 100303. https://doi.org/10.1016/j.forc.2020.100303

Palazzoli, F., Santunione, A. L., Marchesi, F., Verri, P., Vandelli, D., Licata, M., & Silingardi, E. (2021). Cannabinoids determination in brain: A supplemental helpful in postmortem evaluation. *Journal of Analytical Toxicology*, *45*(9), 918–926. https://doi.org/10.1093/jat/bkaa155

Peters, F. T., & Steuer, A. E. (2019). Antemortem and postmortem influences on drug concentrations and metabolite patterns in postmortem specimens. *WIREs Forensic Science*, *1*(1), Article e1297. https://doi.org/10.1002/wfs2.1297

Quenardelle, V., Charles, A.-L., Charloux, A., Raul, J.-S., Wolff, V., & Geny, B. (2025). Young age and concomitant cannabis (THC) and ethanol (EtOH) exposure enhances rat brain damage through decreased cerebral mitochondrial respiration. *Molecules*, *30*(4), Article 918. https://doi.org/10.3390/molecules30040918

Rock, K. L., Englund, A., Morley, S., Rice, K., & Copeland, C. S. (2022). Can cannabis kill? Characteristics of deaths following cannabis use in England (1998–2020). *Journal of Psychopharmacology*, *36*(12), 1362–1370. https://doi.org/10.1177/02698811221115760

Rodda, L. N., Volk, J. A., Moffat, E., Williams, C. M., Lynch, K. L., & Wu, A. H. B. (2018). Evaluation of intraosseous fluid as an alternative biological specimen in postmortem toxicology. *Journal of Analytical Toxicology*, *42*(3), 163–169. https://doi.org/10.1093/jat/bkx096

Saenz, S. R., Lewis, R. J., Angier, M. K., & Wagner, J. R. (2017). Postmortem fluid and tissue concentrations of THC, 11-OH-THC and THC-COOH. *Journal of Analytical Toxicology*, *41*(6), 508–516. https://doi.org/10.1093/jat/bkx033

Santunione, A. L., Palazzoli, F., Verri, P., Vandelli, D., Chiapelli, F., & Silingardi, E. (2023). Cannabinoid stability in postmortem brain samples stored at different temperatures. *Journal of Analytical Toxicology*, *47*(2), 121–128. https://doi.org/10.1093/jat/bkac041

Sastre, C., Bartoli, C., Baillif-Couniou, V., Leonetti, G., & Pelissier-Alicot, A.-L. (2018). Post mortem redistribution of drugs: Current state of knowledge. *Current Pharmaceutical Design*, *23*(36), 5530–5541. https://doi.org/10.2174/1381612823666170622111739

Schaefer, N., Kröll, A.-K., Körbel, C., Laschke, M. W., Menger, M. D., Maurer, H. H., Meyer, M. R., & Schmidt, P. H. (2020). Time- and temperature-dependent postmortem concentration changes of the (synthetic) cannabinoids JWH-210, RCS-4, as well as Δ9-tetrahydrocannabinol following pulmonary administration to pigs. *Archives of Toxicology*, *94*(5), 1585–1599. https://doi.org/10.1007/s00204-020-02707-4

Schwerdt, M. K., & Gill, J. R. (2018). The pitfalls of per se thresholds in accurately identifying acute cannabis intoxication at autopsy. *Forensic Science, Medicine and Pathology*, *14*(4), 497–502. https://doi.org/10.1007/s12024-018-0019-2

Tascon, I., Côté, C., Garneau, B., Desharnais, B., Gosselin, V., & Mireault, P. (2023). Postmortem redistribution of cannabinoids: Statistical analysis of a novel dataset and meta-analysis. *Forensic Science International*, *353*, Article 111873. https://doi.org/10.1016/j.forsciint.2023.111873

Wachholz, P., Celiński, R., Skowronek, R., & Pawlas, N. (2024). Comparative analysis of post-mortem drug concentrations in cerebrospinal fluid and blood. *Forensic Science, Medicine and Pathology*, *21*(1), 23–32. https://doi.org/10.1007/s12024-024-00801-y

Zughaibi, T. A., Alharbi, H., Al-Saadi, A., Alzahrani, A. E., & Al-Asmari, A. I. (2023). 11-Nor-9-carboxy tetrahydrocannabinol distribution in fluid from the chest cavity in cannabis-related post-mortem cases. *Toxics*, *11*(9), Article 740. https://doi.org/10.3390/toxics11090740