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ORIGINAL ARTICLE

Postmortem redistribution of THC in the pig

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Abstract To improve the knowledge of the postmortem redistribution of Δ^9-tetrahydrocannabinol (THC), an animal model using the Large White pig has been developed, whereby 15 pigs received an intravenous injection of THC (200 μg/kg body weight) and were euthanized 2 h after administration. An autopsy was performed on three pigs immediately after being euthanized while the others were stored in supine position at ambient temperature for 6, 15, 24, or 48 h. THC concentration in blood from the vena cava decreased after death whereas left or right cardiac blood concentrations increased. No blood specimens collected from different sites of the carcasses adequately reflected the perimortem THC concentrations. The highest concentrations of THC at anytime were observed in lung tissue, and brain tissue seemed to present the most stable concentrations over time. This study can assist toxicologists in determining which specimens can, most appropriately, be used for interpretation of cannabinoid concentrations in postmortem specimens.

Keywords THC · Cannabinoids · Postmortem redistribution · Animal model · Large White pig

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Introduction

Postmortem drug levels do not necessarily reflect the concentration at the time of death. Interpretation of results is made difficult because of drug instability and postmortem redistribution (PMR) [1]. Data on PMR are available for cocaine, amphetamines, or morphine [2–4] but not for cannabis, the most widely used drug of abuse. Although acute toxicity of Δ^9-tetrahydrocannabinol (THC) is regarded to be low, analysis in fatalities having legal implications is important [5–8].

There is only one case report available about cannabinoid postmortem concentrations, which shows a great variability between tissues [9]. Hilberg et al. studied the variations of postmortem blood THC concentration in rats and demonstrated a postmortem decrease in blood from the inferior vena cava [10]. In vivo tissue distribution of THC has been widely studied using rodents [11, 12] or rabbits [13], animal models that are poorly sensitive to THC and require doses far superior to those used by humans.

We have recently developed a pig model to study the toxicokinetics and tissue distribution of THC [14]. Pigs share anatomical and physiological characteristics with

humans [15]. Furthermore, pigs have already been used as an animal model for studying PMR [16–18]. Physicochemical properties are assumed to be required for a drug to be liable to undergo PMR. This generally applies to weak basic lipophilic drugs [19] with a large volume of distribution (Vd >3 L/kg body weight) [20]. Multiple criteria such as the tissue–plasma partition coefficient (Kp), dissociation constant (*p*Ka), and Vd have to be considered as well [21]. THC is a very lipophilic molecule (log $P_{o/w}$ 7.6) with a *p*Ka of 10.6 and a large Vd of 10 L/kg body weight [22], which suggest that it could be a good candidate for PMR.

Using our previously developed pig model, the aim of this study was to establish whether THC undergoes PMR. We also determined which blood or tissue samples could be more appropriate for interpretation of antemortem/perimortem THC levels.

Materials and methods

Animals

All experiments were performed in accordance with the guidelines of the French Agricultural Office and the legislation governing animal studies.

Animals were Large White male pigs (9–12-week old) weighing 29–50 kg and provided by the research facility center of INRA (Le Magneraud, Surgères, France). Fifteen pigs were used during the experiments. Pigs were individually housed in metabolic cages at a controlled temperature of 21°C. During the experiments, pigs were not fed, but water was allowed ad libitum.

Chemicals

Twenty eight milligrams THC/mL in ethanol was purchased from Sigma-Aldrich (Saint-Quentin-Fallavier, France), deuterated standard (THC-d_3) was purchased from LGC Promochem (Molsheim, France), sodium hydroxide, heptane, and ethyl acetate were purchased from Merck (Darmstadt, Germany), hydrochloric acid was obtained from Carlo Erba (Val de Reuil, France), sodium chloride 0.9% was purchased from B. Braun Medical AG (Emmenbrücke, Switzerland) and *N*,*O*-bis (trimethylsilyl)trifluoroacetamide with 1% trimethylchlorosilane was purchased from Fluka (Buchs, Switzerland).

Administration protocol

In order to facilitate drug injection and multiple blood sampling, the right and left jugular vein of each pig were surgically catheterized at least 1 day before the experiment [14]. The ethanolic solution of THC was diluted in 2 mL of 0.9% NaCl. A single dose of 200 µg of THC per kilogram body weight was administered to each pig by intrajugular injection.

Experiments

Blood samples were collected at 2, 5, 15, 30, 60, and 120 min after injection of THC. All animals were euthanized 2 h after injection in order to allow THC distribution. Euthanasia was performed by KCl injection after NO-induced complete anesthesia. After euthanasia, pigs were left in a dorsal recumbent position at ambient temperature (18–22°C) until autopsy was performed at 0, 6, 15, 24, and 48 h postmortem (three pigs for each postmortem interval (PMI)). Right and left cardiac blood samples were drawn from each ventricle. Blood from the inferior vena cava was drawn just above the kidneys. This sample was limited to 2–3 mL in order to prevent drawing blood from the upper parts of the body. Other samples were collected including: bile, vitreous humor, heart, spleen, kidney, skeletal muscle, fat tissue, right/left lobes of the liver, right/left apex, and base of the lungs. Brain samples were collected from the frontal and occipital cortex, medulla oblongata, olfactory bulb, and cerebellum. For the pigs autopsied at PMI 0, only one fraction of lung and liver tissue was sampled, and postmortem cardiac and inferior vena cava blood samples were not available. All fluid samples were stored at 4°C, and solid samples were kept at –80°C until analysis.

Analytical method

Concentrations of THC were determined using a fully validated method using liquid–liquid extraction and gas chromatography–mass spectrometry [14]. The lower limits of detection (LLOD) and lower limits of quantification (LLOQ) for each matrix are presented in Table 1. The results of this technique were linear up to 1,000 ng/g for lung and up to 200 ng/g for the other matrices (determination coefficients were typically ≥0.99 using a $1/x$ weighted linear least squares regression curve). Intraday and interday imprecision were ≤18.8% and 15.9%, respectively. Inaccuracy, calculated as the percentage difference from the target value, was ≤15.8%.

Statistical analysis

Statistical processing of the data was performed using GraphPad Prism V3.02 from GraphPad Software, San Diego, CA. The Kruskal–Wallis test was used to compare the THC concentration in the postmortem specimens as a function of the PMI. The same test was also used as a nonparametric one-way analysis of variance to compare

Table 1 Lower limits of detection (LLOD) and lower limits of quantification (LLOQ) of Δ^9-tetrahydrocannabinol in the different matrices

	LLOD	LLOQ
Blood (ng/mL)	0.2	0.5
Vitreous humor (ng/mL)	0.1	0.5
Bile (ng/mL)	0.4	1.4
Lung (ng/g)	2.5	7.0
Spleen (ng/g)	1.5	5.1
Cardiac/skeletal muscle (ng/g)	1.3	4.5
Brain (ng/g)	1.6	5.3
Kidney (ng/g)	1.0	3.5
Liver (ng/g)	1.3	4.4
Fat (ng/g)	2.7	9.0

THC concentrations in the different types of blood, followed by Dunn's test to compare each paired type of blood. For each test, p values less than 0.05 were considered to be statistically significant.

Results

Blood THC kinetics before euthanasia

Mean antemortem THC blood concentrations are given in Fig. 1. A mean peak concentration of 87.6±24.1 ng/mL was observed 5 min after injection, and the mean blood THC concentration for the 15 pigs at the time of euthanasia was 7.2±2.8 ng/mL.

Temporal changes of THC concentrations in the postmortem blood samples

Postmortem blood THC concentrations ranged from 0.7 to 10.2 ng/mL (mean 3.2±3.3 ng/mL; median 2.0 ng/mL) in the inferior vena cava, from 1.7 to 37.4 ng/mL (mean 10.9± 9.9 ng/mL; median 8.2 ng/mL) in the right cardiac ventricle, and from 3.2 to 48.8 ng/mL (mean 17.5± 15.5 ng/mL; median 10.5 ng/mL) in the left cardiac ventricle. Results are presented in Fig. 2 as the mean ratio between the postmortem and corresponding antemortem concentration of THC. Left and right cardiac bloods exhibited THC concentrations higher than blood from vena cava. Normalized THC concentrations in inferior vena cava blood samples were markedly less than 1, demonstrating an important postmortem fall in THC levels after death. Changes between antemortem and postmortem concentrations seemed to be already established 6 h after death, and variations with time for each type of blood were not significant (Kruskal–Wallis $p>0.05$). Left cardiac blood samples exhibited higher THC concentrations than the right cardiac blood samples but with a more important variability. Nonparametric one-way analysis of variance (Kruskal–Wallis) showed a significant difference between left cardiac blood ($p<0.001$ Dunn's test) or right cardiac blood ($p<0.05$ Dunn's test) versus blood from inferior vena cava, but no significant difference was found between left and right cardiac blood.

Evolution of THC concentration in the different tissues

Mean THC concentrations in the postmortem biological samples are presented in Table 2. Concentrations were

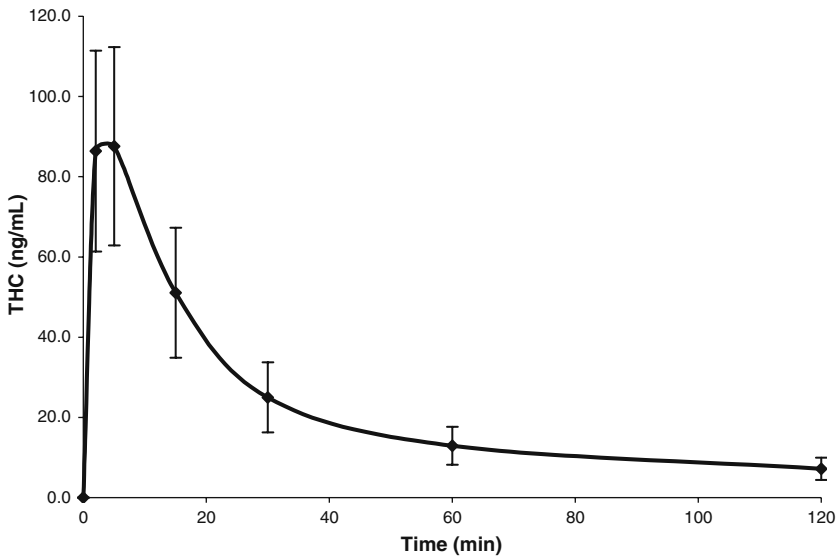

Fig. 1 Blood kinetics in pigs between time of THC injection (200 µg/kg) and time of euthanasia ($n=15$)

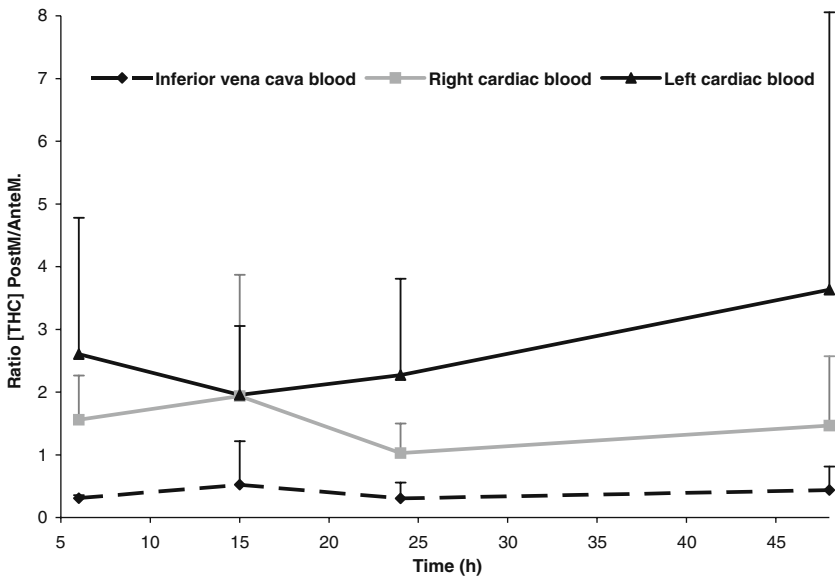

Fig. 2 Evolution of THC concentration ratios in the different bloods. Ratios are measured as THC concentration in postmortem blood/THC concentration in antemortem blood (n=3)

highest in lung specimens (range 217.1 to 925.5 ng/g) whereas low concentrations were present in bile, vitreous humor, and liver. Spleen, muscle, and heart exhibited medium THC concentrations at PMI 0 (around 10–15 ng/g) and showed an important fall with increasing PMI. Kidney and fat tissue THC concentrations followed a similar pattern (from 40 to 20 ng/g) over the 48-h experiment. Brain THC concentrations were very similar in the different areas sampled and showed a tendency to increase over time. Kruskal–Wallis test has been performed on each individual matrix with time as a variable but failed to demonstrate any variation related to the PMI (p>0.05). However, marked but not significant tendencies to decreased THC levels were observed for muscle (p=0.066) and heart (p=0.114) tissues whereas a tendency to increased THC levels was revealed for brain (p=0.252).

Figure 3 shows the percentage of THC remaining in brain, fat, heart, lung, kidney, and skeletal muscle as a function of the PMI. Muscle showed a rapid (30.2% of THC remaining at 6 h) and complete (0% after 48 h) decrease in THC concentration; heart and kidney revealed a similar evolution with THC levels remaining at around 40–50% after 24–48 h. Fat with a slightly different evolution also maintained a THC level at around 50% after 48 h. Brain appeared to be the only tissue with a marked increase in THC remaining over time. This increase, slight at the early stages (112.9–134.0% of THC remaining) tended to be more important after 48 h (160.0% of THC remaining). Among the five areas of the brain selected, only occipital cortex seemed to undergo less variation than others brain areas (Table 2). The other areas reflected the global evolution observed for the entire brain.

Discussion

Time course following injection of THC until euthanasia of the pigs was similar to the mean peak concentration and to the concentration range of 5–10 ng/mL after 2 h observed in human plasma following injection of 5 mg of THC [23].

The fact that postmortem THC concentrations were higher in cardiac blood than in blood from inferior vena cava can easily be explained. The accumulation of THC in lung tissue creates a diffusion gradient toward surrounding areas and especially to the heart and cardiac blood. Two mechanisms could be involved to explain the high THC concentration in postmortem cardiac blood, diffusion from lung tissue through the myocardium or inside the vessels from pulmonary blood to cardiac blood [24]. Redistribution via blood is more likely to be involved considering the low THC concentration observed in cardiac muscle.

Changes in THC concentration in the postmortem blood appeared to be an early phenomenon. Similarly, with rats and amitriptyline, Hilberg et al. demonstrated that redistribution from lung tissue to heart blood occurs rapidly within the first 2 h after death [25]. The postmortem fall in THC concentration in the blood from inferior vena cava noticed in our experiments with pigs is not a classical finding and has not been observed with amitriptyline [25] and clozapine [17]. The same decrease in blood from the inferior vena cava of rats was reported by Hilberg et al. [20]. The reasons for the decrease in THC concentration are unclear. It is likely that the equilibrium between blood and tissue was not yet reached 2 h after injection even though the kinetics before euthanasia seemed to indicate that the elimination phase was ongoing. It is also possible that this equilibrium

Table 2 Concentrations of THC (nanogram per gram) in the different biological samples as a function of the PMI (n=3)

PMI (h)		Lung R base	Lung L base	Lung R apex	Lung L apex	Liver R lobe	Liver L lobe	Kidney	Spleen	Muscle	Heart	Fat	Brain[e]	Frontal C.	Occipital C.	Olfactory B.	Medulla O.	Cerebellum	Vitreous H.	Bile
0	**Mean**	**476.7**[a]				**2.8**[a]		**42.8**	**11.6**	**14.1**	**14.8**	**43.9**	**14.8**	**15.5**	**20.9**	**11.8**	**9.4**	**16.4**	**0.2**	**1.4**
	SD	212.6				4.8		30.5	9.4	7.3	4.5	12.4	3.7	4.9	5.7	3.1	8.7	3.2	0.3	1.4
6	**Mean**	**633.2**	**301.8**	**574.5**	**448.5**	**6.4**	**7.8**	**38.9**	**<LLOQ**	**4.2**	**12.8**	**31.5**	**19.8**	**20.0**	**23.2**	**15.9**	**16.3**	**23.9**	**<LLOQ**	**7.5**
	SD	451.7	95.8	415.8	200.9	6.9	8.0	15.1	N/A	7.3	4.2	29.9	3.7	2.7	7.6	2.1	4.7	5.9	N/A	9.0
15	**Mean**	**596.8**	**925.5**	**651.2**	**356.3**	**2.1**	**<LLOQ**[b]	**24.8**	**<LLOQ**	**1.7**	**9.6**	**33.0**	**16.8**	**18.2**	**18.8**	**18.5**	**10.3**	**17.8**	**<LLOQ**	**<LLOQ**
	SD	94.8	393.4	385.2	239.5	3.6	N/A[c]	21.9	N/A	3.0	1.8	11.5	1.8	1.0	1.2	8.4	3.0	0.4	N/A	N/A
24	**Mean**	**217.1**	**270.3**	**300.7**	**399.2**	**4.7**	**4.0**	**15.9**	**<LLOQ**	**2.4**	**5.5**	**39.1**	**16.7**	**19.5**	**19.8**	**10.8**	**12.4**	**21.0**	**<LLOQ**	**2.4**
	SD	162.2	121.2	286.7	66.5	8.2	6.9	6.6	N/A	1.9	7.8	19.7	8.5	6.7	5.4	14.8	2.7	14.8	N/A	0.4
48	**Mean**	**248.7**	**738.0**	**542.6**	**548.7**	**7.4**	**5.7**	**22.5**	**<LLOQ**	**<LLOD**[d]	**7.0**	**20.7**	**24.4**	**29.6**	**24.2**	**21.7**	**25.1**	**21.3**	**<LLOQ**	**2.3**
	SD	127.9	562.9	446.8	246.8	4.7	4.2	22.0	N/A	N/A	1.8	12.6	3.8	15.8	8.8	5.5	3.5	3.7	N/A	2.2

THC Δ^9-tetrahydrocannabinol, *PMI* postmortem interval, *LLOQ* lower limits of quantification, *LLOD* lower limits of detection, *R* right, *L* left, *C*. cortex, *B*. bulb, *O*. oblongata, *H*. humor

[a] For pigs at PMI=0, only one fraction of lung and liver has been sampled

[b] <LLOQ = mean value below the lower limit of quantification of the method

[c] N/A = standard deviation not applicable

[d] <LLOD = mean value below the lower limit of detection of the method

[e] Values for brain are the mean of the five areas collected

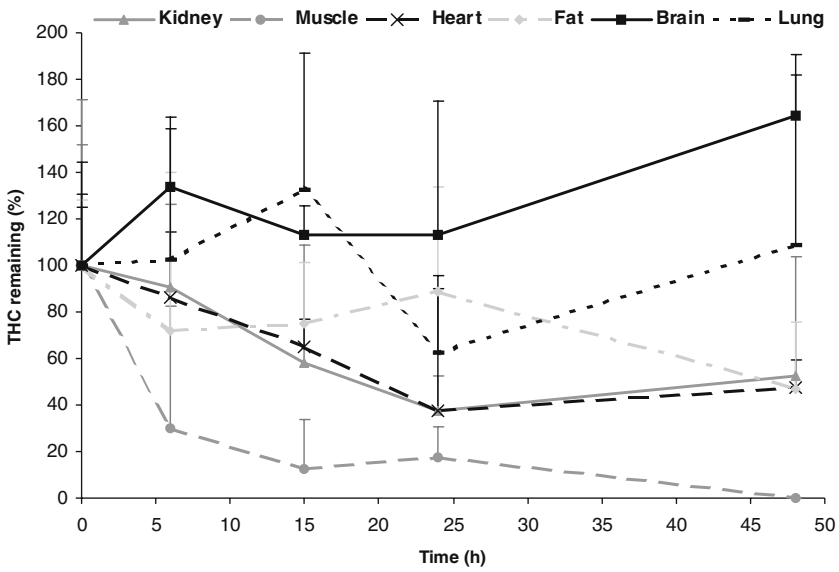

Fig. 3 Evolution of percentage of THC remaining in the different tissues (n=3). Values for each matrix have been normalized taking the value for PMI 0 as 100%

between blood and tissues was modified after death due to the arrest of circulation and the decrease in intracellular pH [26]. An important conclusion from this study is that neither the postmortem cardiac blood nor the postmortem blood from inferior vena cava is a good indicator of the blood THC concentration at the time of death. In forensic cases, the safest way to interpret results from postmortem blood is probably by using an interval with peripheral postmortem blood as the low value and cardiac postmortem blood (ideally right cardiac blood) as the high value. THC concentration in blood at the time of death is most likely included in that interval, the width of which is representing the extent of PMR.

Analysis of THC in different tissues gives an important indication of which organ could be the origin of the PMR. Concentrations of THC in lungs are 10 to 100 times higher than in the other organs. As the lungs are the most perfused organs of the body, they accumulate THC. Active transport of drugs into lung tissue has also been proposed as another mechanism of accumulation [27]. In forensic cases, lung tissue should be the specimen of choice in the absence of blood to detect cannabis consumption.

Fat is obviously an interesting matrix for the detection of cannabis use. The high lipophilicity of THC contributes to its accumulation in fat tissue [28], and this retention could be at the origin of the prolonged half-life among heavy users [29]. Despite the fact that fat is a difficult matrix to analyze, it could provide interesting information to differentiate between occasional and heavy users of cannabis. While vitreous humor is a useful specimen for alcohol analysis [30], its use to detect recent consumption of THC is limited. THC seems to spread scarcely in vitreous humor which is obviously due to its high protein binding [31].

When dealing with PMR studies, brain tissue has to be considered as a particularly important organ. Brain is anatomically isolated from the other organs; its metabolic activity is lower than in blood, and putrefaction processes and decomposition are delayed compared to abdominal organs [32]. Moreover, the central nervous system is the place where each drug of abuse establishes its effects, and it has been reported that THC could still be present in the brain while absent in the blood [33]. Levels of THC remaining in the entire brain of pigs were between 110% and 165%, the latter level being observed for the longer PMI (48 h). In brain and in blood, THC concentrations are of the same order, and irrespective of the PMI brain might be the best reflection of perimortem THC concentrations.

Conclusion

In conclusion, this study has confirmed that THC is a molecule subject to PMR. Temporal changes in THC concentrations observed in blood of pigs (increase in cardiac blood and decrease in blood from inferior vena cava) are of major interest in forensic toxicology. It underlines the importance of knowing the postmortem interval and the localization of the sample in order to interpret THC concentrations in forensic cases. If blood specimens from different origin are available, analysis of both cardiac and peripheral blood is recommended. Among other specimens interesting to analyze, lung exhibited the highest concentrations and brain tissue, the most stable concentrations.

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References

1. Pounder DJ, Jones GR (1990) Post-mortem drug redistribution—a toxicological nightmare. Forensic Sci Int 45:253–263
2. Hearn WL, Keran EE, Wei HA, Hime G (1991) Site-dependent postmortem changes in blood cocaine concentrations. J Forensic Sci 36:673–684
3. De Letter EA, Belpaire FM, Clauwaert KM, Lambert WE, Van Bocxlaer JF, Piette MH (2002) Post-mortem redistribution of 3,4-methylenedioxymethamphetamine (MDMA, "ecstasy") in the rabbit. Part I: experimental approach after in vivo intravenous infusion. Int J Legal Med 116:216–224
4. Gerostamoulos J, Drummer OH (2000) Postmortem redistribution of morphine and its metabolites. J Forensic Sci 45:843–845
5. Bachs L, Morland H (2001) Acute cardiovascular fatalities following cannabis use. Forensic Sci Int 124:200–203
6. Huestis MA (2002) Cannabis—effects on human behavior and performance. Forensic Sci Rev 14:15–59
7. Kelly E, Darke S, Ross J (2004) A review of drug use and driving: epidemiology, impairment, risk factors and risk perceptions. Drug Alcohol Rev 23:319–344
8. Mura P, Kintz P, Ludes B et al (2003) Comparison of the prevalence of alcohol, cannabis and other drugs between 900 injured drivers and 900 control subjects: results of a French collaborative study. Forensic Sci Int 133:79–85
9. Kudo K, Nagata T, Kimura K, Imamura T, Jitsufuchi N (1995) Sensitive determination of Δ^9-tetrahydrocannabinol in human tissues by GC-MS. J Anal Toxicol 19:87–90
10. Hilberg T, Ripel A, Slordal L, Bjorneboe A, Morland J (1999) The extent of postmortem drug redistribution in a rat model. J Forensic Sci 44:956–962
11. Leighty EG (1973) Metabolism and distribution of cannabinoids in rats after different methods of administration. Biochem Pharmacol 22:1613–1621
12. Harvey DJ (1988) In vivo metabolism of (+)-trans-delta-9-tetrahydrocannabinol in the mouse. Biomed Environ Mass Spectrom 15:117–122
13. Leuschner JT, Harvey DJ, Bullingham RE, Paton WD (1986) Pharmacokinetics of delta-9-tetrahydrocannabinol in rabbits following single or multiple intravenous doses. Drug Metab Dispos 14:230–238
14. Brunet B, Doucet C, Venisse N, Hauet T, Hébrard W, Papet Y, Mauco G, Mura P (2006) Validation of Large White pig as an animal model for the study of cannabinoids metabolism: application to the study of THC distribution in tissues. Forensic Sci Int 161:169–174
15. Tumbleson ME (1986) Swine in biomedical research. In: Tumbleson ME (ed) Swine in biomedical research. Plenum Press, New York, p 5
16. Hilberg T, Ripel A, Smith AJ, Slordal L, Morland J, Bjorneboe A (1998) Postmortem amitriptyline pharmacokinetics in pigs after oral and intravenous routes of administration. J Forensic Sci 43:380–387
17. Flanagan RJ, Amin A, Seinen W (2003) Effect of post-mortem changes on peripheral and central whole blood and tissue clozapine and norclozapine concentrations in the domestic pig (Sus scrofa). Forensic Sci Int 132:9–17
18. Crandall CS, Kerrigan S, Aguero RL, Lavalley J, McKinney PE (2006) The influence of collection site and methods on post-mortem morphine concentrations in a porcine model. J Anal Toxicol 30:651–658
19. Moriya F, Hashimoto Y (1999) Redistribution of basic drugs into cardiac blood from surrounding tissues during early-stages postmortem. J Forensic Sci 44:10–16
20. Hilberg T, Rogde S, Morland J (1999) Postmortem drug redistribution—human cases related to results in experimental animals. J Forensic Sci 44:3–9
21. Pélissier-Alicot AL, Gaulier JM, Dupuis C, Feuerstein M, Leonetti G, Lachatre G, Marquet P (2006) Post-mortem redistribution of three beta-blockers in the rabbit. Int J Legal Med 120:226–232
22. Moffat AC, Osselton MD, Widdop B (2004) Clarke's analysis of drugs and poisons, 3rd edn. Pharmaceutical Press, London
23. Ohlsson A, Lindgren JE, Wahlen A, Agurell S, Hollister LE, Gillespie HK (1980) Plasma delta-9 tetrahydrocannabinol concentrations and clinical effects after oral and intravenous administration and smoking. Clin Pharmacol Ther 28:409–416
24. Hilberg T, Morland J, Bjorneboe A (1994) Postmortem release of amitriptyline from the lungs; a mechanism of postmortem drug redistribution. Forensic Sci Int 64:47–55
25. Hilberg T, Bugge A, Beylich KM, Ingum J, Bjørneboe A, Mørland J (1993) An animal model of postmortem amitriptyline redistribution. J Forensic Sci 38:81–90
26. Pélissier-Alicot AL, Gaulier JM, Champsaur P, Marquet P (2003) Mechanisms underlying postmortem redistribution of drugs: a review. J Anal Toxicol 27:533–544
27. Yoshida H, Okumura K, Kamiya A, Hori R (1989) Accumulation mechanism of basic drugs in the isolated perfused rat lung. Chem Pharm Bull 37:450–453
28. Johansson E, Norén K, Sjövall J, Halldin MM (1989) Determination of delta 1-tetrahydrocannabinol in human fat biopsies from marihuana users by gas chromatography–mass spectrometry. Biomed Chromatogr 3:35–38
29. Johansson E, Agurell S, Hollister LE, Halldin MM (1988) Prolonged apparent half-life of delta 1-tetrahydrocannabinol in plasma of chronic marijuana users. J Pharm Pharmacol 40:374–375
30. Briglia EJ, Bidanset JH, Dal Cortivo LA (1992) The distribution of ethanol in post-mortem blood specimens. J Forensic Sci 37:991–998
31. Garrett ER, Hunt CA (1974) Physiochemical properties, solubility, and protein binding of delta-9-tetrahydrocannabinol. J Pharm Sci 63:1056–1064
32. Stimpfl T, Reichel S (2007) Distribution of drugs of abuse within specific regions of the human brain. Forensic Sci Int 170:179–182
33. Mura P, Kintz P, Dumestre V, Raul S, Hauet T (2005) THC can be detected in brain while absent in blood. J Anal Toxicol 29:842–843