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Increased Cannabinoids Concentrations Found in Specimens From Fatal Aviation Accidents Between 1997 and 2006

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16. Abstract The Civil Aerospace Medical Institute's toxicology laboratory receives biological specimens from more than 90% of all fatal aviation accidents that occur in the United States and its territories. As a part of the routine analysis of pilot specimens, the laboratory tests all cases for the presence of marijuana (cannabis). The National Institute on Drug Abuse (NIDA) and the Office of National Drug Control Policy (ONDCP) reported a 1.5-fold increase in the delta-9-tetrahydrocannabinol (THC) content of street cannabis seizures from 1997-2001 to 2002-2006. This study was conducted to compare the changes, over those years, in blood and urine cannabinoid concentrations with the potency of THC reported in the cannabis plant. In our laboratory, cannabinoids are screened using radioimmunoassay (RIA) for blood and fluorescence polarization immunoassay (FPIA) for urine and confirmed using GC/MS. A total of 95 individuals were found to be using cannabis from a total number of 2769 (3.4%) individuals tested over the period 1997 through 2006. Blood was received for analysis from 1676 fatally injured individuals. Urine was received for analyses from 1650 fatalities. Cannabinoids were found in 88 of the 1676 (5.3%) blood specimens received for analysis, and 64 of the 88 were from pilots. Cannabinoids were found in 68 of the 1650 (4.1%) urine specimens received for analysis, and 57 of the 68 were from pilots. Other impairing drugs were found in 39% of the cannabinoids-positive individuals. The mean concentration of THC in blood for 1997-2001 was 2.7 ng/mL; for 2002-2006, it was 7.2 ng/mL, a 2.7-fold increase in the mean THC concentration of specimens from aviation fatalities, compared to a 1.5-fold increase in cannabis potency reported by the NIDA and ONDCP over the 10 years of this study. The median age for cannabis users was 42 years (range 18-72) for aviation fatalities. For all blood and urine specimens tested from aviation fatalities, the mean age of the individuals with negative test results was 50 years (range 14-92). More than half of the fatalities tested were 50 years or older, whereas 80% of the positive cannabis users were under 50. THC concentrations in blood ranged from 0 ng/mL to 68 ng/mL, with a mean concentration of 5.5 ng/mL. Concentrations of 11-nor-9-carboxy-THC (THC-COOH) found in blood ranged from 0 ng/mL to 179 ng/mL, with a mean concentration of 17.5 ng/mL. Urine concentrations for THC-COOH ranged from 2 to 1,113 ng/mL, with a mean concentration of 137.9 ng/mL.			
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INCREASED CANNABINOIDS CONCENTRATIONS FOUND IN SPECIMENS FROM FATAL AVIATION ACCIDENTS BETWEEN 1997 AND 2006

INTRODUCTION

Although it remains the most commonly used illicit drug in the United States cannabis use has declined slightly over the past 10 years.^{1,2} However, the potency of cannabis, as measured by delta-9-tetrahydrocannabinol (THC) concentrations, has nearly doubled from 1997 to 2006.³ This increased potency could result in higher concentrations of THC and incidence of impairment in persons working in the transportation industry. It has also been reported that marijuana use disorders among cannabis users, which are already the most prevalent illicit substance use disorders in the population, increased significantly ($P=0.002$) between 1991-1992 and 2001-2002 in the absence of increased frequency and quantity of cannabis use, suggesting that concomitant increased cannabis potency may have contributed to the rising rates of cannabis use disorders.⁴

Recent studies have shown that cannabis users choose to smoke high-potency cannabis more often than low-potency cannabis.⁵ High-potency cannabis users will generally increase their average THC intake.⁶ There are contradictory reports that subjects do not regulate their cannabis smoke intake in response to changes in cannabis potency⁷ and that they do titrate their intake.⁸ If cannabis users do titrate the amount of cannabis used based on its potency, one would not expect a significant increase in the concentration of cannabinoids found in blood samples collected over a 10-year period during which the potency of the cannabis significantly increased.

Most of the earlier performance studies used low-potency cannabis, compared to the potency of cannabis available today, and probably do not reflect the performance impairment potential of high-potency cannabis.⁹ Studies conducted with high-potency cannabis have demonstrated consistent impairment of executive function, tracking performance, and motor impulse control.⁶ The impairment was shown to last for up to 6 hours after smoking. There is other recent evidence that the use of cannabis is not harmless.^{4,10,11}

Research has shown that THC concentrations in blood between 3.5-5.0 ng/mL (plasma 7-10 ng/mL) have an impairing effect on drivers equivalent to a blood alcohol concentrations 0.05%.¹² The FAA prohibits pilots from operating an aircraft with blood alcohol concentrations at or above 0.04%. That raises the question of how many

aviation accidents are found with pilots having blood THC concentrations at or above the impairing range, compared to fatal aviation accidents that occurred prior to the availability of high-potency cannabis.

This study was undertaken to compare the change in reported cannabis potency with changes in the concentrations of THC and its 11-nor-9-carboxy-THC (THC-COOH) metabolite found in urine and blood from fatal aviation accidents during the period from 1997 to 2006.

MATERIALS AND METHODS

The Civil Aerospace Medical Institute (CAMI) receives biological fluids and tissues for toxicology analysis from all aviation accidents that occur nationwide. Blood specimens received from pilots are screened for THC-COOH by radioimmunoassay (RIA) and urine specimens by fluorescence polarization immunoassay (FPIA). Solid phase extraction is used to isolate THC and THC-COOH from blood and urine. The confirmation and quantitation of THC-COOH in urine is performed using gas chromatography and electron impact mass spectrometry (GC/MS). THC and THC-COOH in blood are confirmed and quantitated by negative-ion chemical ionization GC/MS, based on a modification of a procedure published in 1983.¹³ The procedure used to analyze cannabinoids includes deuterated internal standards and has a limit of detection and a limit of quantitation of 1 ng/mL in blood and urine.

A 10-year period from 1997 to 2006 was selected for this study to correlate with data reported by the National Institute on Drug Abuse (NIDA) and the Office of National Drug Control Policy (ONDCP) on cannabis potency.³ Cannabinoids concentrations in blood and urine were compared with the reported potency of cannabis during the same time period.

RESULTS

The principal findings of this study are contained in Tables 1-6. From 1997 through 2006, a total of 95 (3.4%) individuals were found to have used cannabis of 2769 individuals tested. Of the 95 cannabinoids-

Table 1. Demographics of the Study Subjects and Number of Cannabinoids-Positive and Negative Results.

Category	N	Age Mean	SD	Age Median	Age Range
Males Positive	87	40	12	42	18-72
Males Negative	2543	50	15	51	14-92
Total	2630	50	15	50	14-92
Females Positive	8	36	9	39	24-45
Females Negative	120	44	15	44	17-77
Total	128	44	15	44	17-77
Undesignated Positive	0	NA	NA	NA	NA
Undesignated Negative	11	36	9	39	19-44
Total	11	36	9	39	19-44
All Total Positive	95	40	12	42	18-72
All Total Negative	2674	50	15	51	14-92
All Total	2769	49	15	50	14-92

Table 2. Cannabinoids-Positive Results in Blood by Year of Study.

Year	N	Δ9 THC ng/mL Blood				TCH-COOH ng/mL Blood			
		Mean	SD	Median	Span	Mean	SD	Median	Span
1997	9	1.3	2.6	0.0	0.0-8.0	11.6	13.0	9.0	1.0-41.0
1998	7	0.9	1.9	0.0	0.0-5.0	4.7	4.2	2.0	1.0-11.0
1999	7	3.1	4.3	2.0	0.0-12.0	14.7	15.5	11.0	1.0-42.0
2000	8	3.9	4.7	2.0	0.0-13.0	9.1	16.2	2.0	1.0-48.0
2001	9	4.2	7.3	1.0	0.0-19.0	18.1	21.1	6.0	1.0-53.0
2002	6	1.0	2.0	0.0	0.0-5.0	3.8	4.8	1.0	0.0-11.0
2003	19	7.8	16.3	2.0	0.0-68.0	11.0	7.4	12.0	1.0-22.0
2004	7	9.9	15.4	2.0	0.0-37.0	20.9	32.5	10.0	1.0-92.0
2005	7	2.7	2.4	2.0	0.0-7.0	25.9	44.1	8.0	1.0-122.0
2006	9	14.8	20.5	5.0	2.0-65.0	56.0	67.3	28.0	8.0-179.0
Totals	88	5.5	11.7	1.5	0.0-68.0	17.5	30.6	8.5	0.0-179.0

Table 3. Cannabinoids-Positive Results in Urine by Year of Study.

Year	N	TCH-COOH ng/mL Urine			
		Mean	SD	Median	Span
1997	10	98.0	211.8	26.0	2.0-695.0
1998	6	31.5	36.6	14.0	3.0-100.0
1999	8	98.5	161.5	43.5	10.0-493.0
2000	5	68.0	57.2	37.0	18.0-147.0
2001	6	142.0	131.1	83.0	40.0-388.0
2002	6	52.2	47.1	41.5	9.0-142.0
2003	11	113.9	178.6	29.0	3.0-600.0
2004	3	316.7	465.1	86.0	12.0-852.0
2005	6	182.2	203.8	87.0	31.0-543.0
2006	7	373.9	382.7	308.0	8.0-1113.0
Totals	68	137.9	218.9	45.5	2.0-1113.0

Table 4. Summary of Results in Urine for Cannabinoids and Other Impairing Drugs by Year of Study.

Year	Cases Tested for Cannabinoids	Negative Cannabinoids	Positive Cannabinoids	Cannabinoids & Other Drugs
1997	191	181	10	5
1998	176	170	6	2
1999	162	154	8	2
2000	163	158	5	2
2001	162	156	6	1
2002	150	144	6	1
2003	187	176	11	4
2004	159	156	3	3
2005	163	157	6	3
2006	137	130	7	3
Totals	1650	1582	68	26

Table 5. Summary of Results in Blood for Cannabinoids and Other Impairing Drugs by Year of Study.

Year	Cases Tested for Cannabinoids	Negative Cannabinoids	Positive Cannabinoids	Positive Cannabinoids & Other Drugs
1997	178	169	9	5
1998	140	133	7	2
1999	165	158	7	2
2000	163	155	8	3
2001	157	148	9	1
2002	168	162	6	1
2003	197	178	19	9
2004	179	172	7	5
2005	167	160	7	2
2006	162	153	9	5
Totals	1676	1588	88	35

Table 6. Ratio of Blood to Urine Cannabinoids.

Urine-Range ng/mL	Mean Blood THC	Mean Blood THC-COOH	Mean Urine THC-COOH	Blood/Urine THC-COOH	Blood THC /Urine THC-COOH	N
0-9.0	0.8	3.5	4.9	1	6	8
10-14.0	5	4	12.1	3	2	8
Mean	2.9	3.8	8.5	2	4	8
SD	3.0	0.4	5.1	1.4	2.8	0
15.0-30.0	1.9	1.9	21.8	11	11	8
31.0-60.0	1	6.4	40.5	6	41	12
61.0-100.0	1.1	10.6	82.2	8	75	13
100.0-400.0	3.4	17.4	201.1	12	59	11
400.0-1113.0	13	55.4	662.3	12	51	8
Mean	4.1	18.3	201.6	9.8	47.4	10
SD	5.1	21.5	266.8	2.7	23.8	2.3

positive individuals, 39% were also found positive for other impairing drugs. Blood was received for analysis from 1676 fatalities. Urine was received for analysis from 1650 fatally injured individuals. Cannabinoids were found in 88 (5.3%) of the 1676 blood specimens received for analysis, and 64 of these were from pilots. Cannabinoids were found in 68 (4.1%) of the 1650 urine specimens received for analysis; 57 of these were from pilots.

The median age for cannabis users was 42 years among the fatally injured aviation individuals, with a range from 18 to 72 (Figure 1). For negative cannabinoids in blood and urine specimens tested, the median age was 50 years, with a span from 14 to 92. More than half of the fatally injured persons tested were 50 years or older, whereas 80% of the cannabis users were under 50.

THC concentrations in blood ranged from 0 to 68ng/mL, with a mean of 5.5 ng/mL. THC-COOH concentrations in blood ranged from 0 to 179 ng/mL, with a mean of 17.5 ng/mL. Urine concentrations of THC-COOH ranged from 2 to 1,113 ng/mL, with a mean of 137.9 ng/mL.

Between 1997 and 2001, 8 positive THC cases of 55 positive cannabinoids cases in blood were at or above 3.5 ng/mL, while 20 of the reported 51 positive cannabis cases in blood from 2002 to 2006 were at or above 3.5 ng/mL. This is more than a two-fold increase over those years with lower cannabis potency.

The data indicated an approximately 1/10 blood/urine THC-COOH ratio for urine THC-COOH concentrations above 15 ng/mL. For urine THC-COOH concentrations at or below 15 ng/mL, there was an approximately 1/2 blood/urine THC-COOH ratio. The ratio of the mean blood THC concentration to the mean urine THC-COOH concentration for urine specimens with

THC-COOH concentrations at or below 15 ng/mL was 1/3 and 1/50 for concentrations above 15 ng/mL.

The mean concentration of THC in blood for the period 1997-2001 was 2.7 ng/mL it was 7.2 ng/mL for 2002-2006, a 2.7-fold increase in the mean THC concentration of specimens from aviation fatalities. The annual mean THC concentration found in blood increased from 1.3 ng/mL in 1997 to 14.8 ng/mL in 2006, an 11.3-fold increase. The annual maximum THC concentration found in blood increased from 8 ng/mL in 1997 to 65 ng/mL in 2006, an 8.1-fold increase.

The mean concentration of THC-COOH in blood for the period 1997-2001 was 11.6 ng/mL, and for 2002-2006 it was 23.5 ng/mL, a 2.0-fold increase in the mean THC-COOH concentration of specimens from aviation fatalities. The annual mean THC-COOH concentration found in blood increased from 11.6 ng/mL in 1997 to 56.0 ng/mL in 2006, a 4.8-fold increase. The annual maximum THC-COOH concentration found in blood increased from 41 ng/mL in 1997 to 179 ng/mL in 2006, a 4.4-fold increase.

Urine specimens were received from 740 fatally injured pilots designated as airline transport or commercial pilots, and 14 (1.9%) of the commercial pilot cases exceeded the DOT workplace drug testing urine THC-COOH confirmation threshold (15 ng/mL).¹⁴

No cannabinoids were found in specimens from the airline transport pilots tested. Eight (57%) fatally injured commercial pilots (including agricultural pilots) found with a urine THC-COOH in excess of the DOT workplace drug testing urine threshold were flying private planes. Urine specimens from fatally injured agricultural pilots (Part 137) were found to exceed the DOT workplace drug testing threshold THC-COOH in 5 (36%)

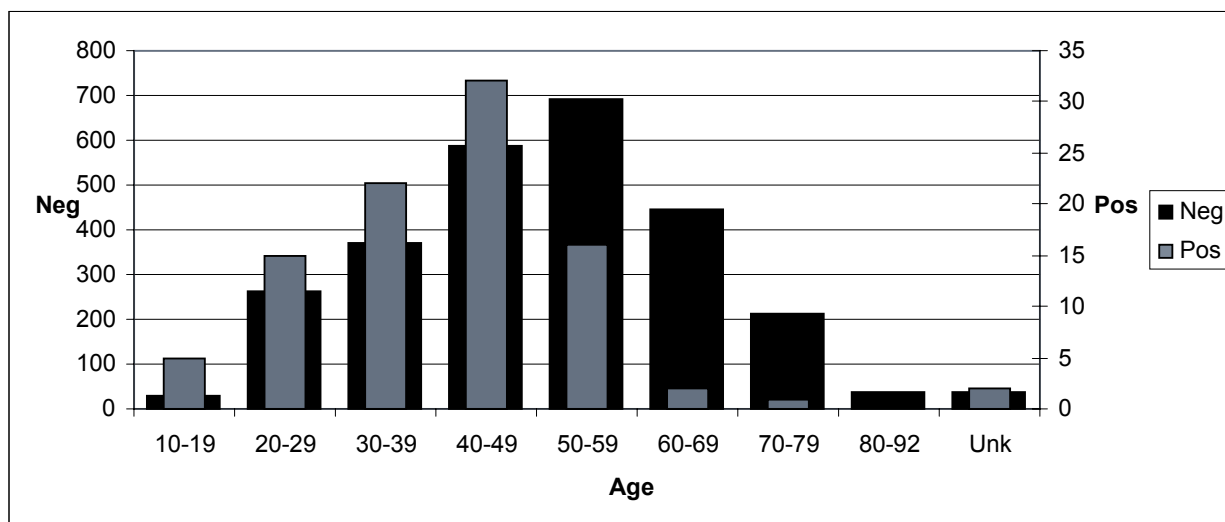


Figure 1. Graphic display of age distribution for all fatal pilots and cannabis users.

of the THC-COOH positive cases. One fatally injured commercial air taxi pilot (Part 135) was found to exceed the DOT workplace drug testing urine threshold for THC-COOH.

In the present study, 61 of 2,769 cases (2.2%) were found to have ethanol at or above 40 mg/dL (0.04%) in blood or urine.

DISCUSSION

The 2.7-fold increase in the mean blood THC concentration found in this study for the 1997-2001 and 2002-2006 periods compares to a 1.5-fold increase in the mean THC concentration of cannabis reported by the National Drug Intelligence Center (NDIC) for the 1997-2001 and 2002-2006 periods. The reasons for this difference are presently unknown. The analytical toxicology procedures for THC and THC-COOH used at CAMI remained the same during the period of this study, as did the quality assurance and quality control procedures, including internal and external “blind” performance testing.

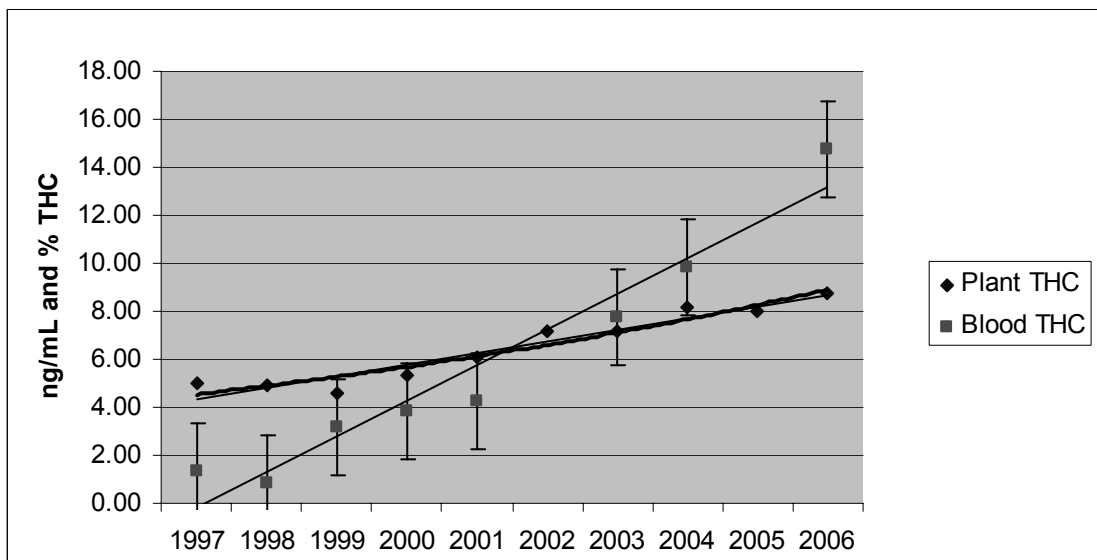
In 2006, 0.05 % of the individuals (flight crewmembers) tested in the FAA aviation industry random drug testing program were found to be positive for marijuana;¹⁵ 6.0% of the commercial pilots tested in the CAMI forensic drug testing laboratory (fatal aviation accident pilots) were positive for THC-COOH at or above the threshold of 15 ng/mL THC-COOH in urine. The commercial pilots tested in the CAMI forensic toxicology department for 2006 were flying private planes (Part 91) or crop dusters (Part 137). Not all commercial pilots (agricultural pilots,

for example) are required to participate in the random drug testing program.

Government agencies and the scientific literature repeatedly reported that the potency of cannabis has been increasing over the 10 years of this study.^{3,16,17} The mean concentration of THC in blood specimens from fatal aviation accidents tested by CAMI has also increased over the last 10 years, but at a greater rate than marijuana potency (Figure 2). Research conducted in Sweden also found an increase in the mean concentration of THC in blood from 1.8 to 2.3 ng/mL in a 10-year (1995-2004) study of drug impaired drivers.¹⁸

Controlled laboratory experiments on driving-related skills reported in the literature have shown that THC concentrations between 2 and 5 ng/mL in whole blood are associated with driver impairment.¹⁹ Serum THC concentrations between 7-10 ng/mL (whole blood, approximately 3.5-5.0 ng/mL) have been compared to a blood alcohol concentration of 0.05%,¹² which exceeds the DOT alcohol threshold of 0.04% (BAC) for transportation workers in safety-sensitive positions. It is clear that the use of high-potency cannabis could significantly alter the performance of an individual, assuming the blood THC concentrations increase correspondingly.

In a study in Norway, 589 (2.0%) samples of approximately 30,000 samples from impaired drivers were found to contain only THC as the impairing drug.²⁰ The Norway epidemiological study indicated an association of driving impairment in individuals at or above 2.5 ng/mL THC in blood and found no impairment at blood THC concentrations at or below 1.9 ng/mL in suspected drugged drivers.²⁰ This is consistent with earlier findings



Note: Blood THC results for 2002 and 2005 were removed as outliers from this graph.

Figure 2. Increase in blood THC (ng/mL) and cannabis potency (% THC) 1997-2006.

of a linear, dose-related, physiological response to THC.²¹ “Furthermore, drivers with blood THC concentrations above 3 ng/mL had an increased risk for being judged impaired compared to drivers with lower concentration ranges.”²⁰ In our research, we found that approximately 46 % (22/48) of the blood samples positive for THC from 2002-2006 had concentrations of THC greater than 3.5 ng/mL, whereas only 25 % (10/40) exceeded that concentration between 1997 and 2001.

Although there were only 95 cannabinoids-positive cases reported in this study, cannabis use may be more prevalent in the driving population and in other modes of transportation. A 10-year study from 1995 to 2004 of drug impaired drivers in Sweden found that 8,794 drivers had THC in their blood;¹⁸ constituting a proportion rising from 18 to 29 % of all tested specimens during that decade. This suggests that the prevalence of THC in the driving population is far higher than we found in aviation fatalities.

A study of 1,079 commercial tractor-trailer drivers in the State of Washington found that 4.3% of the drivers were using cannabis, while 1.3 % of the drivers were using alcohol;²² cannabis use in truck drivers was 3.3 times as prevalent as alcohol use in this 2002 report.²² In our study of aviation fatalities cannabis use was found to be 1.7 times greater than alcohol use at or above 40 mg/dL in blood or urine. These findings are contrary to the widely held perception that alcohol is the most commonly abused drug in transportation. It is also important to recognize that some of the alcohol positive cases found in aviation fatalities in this study could have been the result of postmortem ethanol formation.²³

Cannabis use in conjunction with other impairing substances such as alcohol has been reported to significantly increase the driving impairment of an individual and to cause impairment by cannabis at much lower concentrations than 3.5 ng/mL of THC in whole blood.²⁴ This study found that 39% of the positive cannabinoids cases were also positive for other impairing substances.

In a study of THC positive drivers in Sweden, the mean age was reported as 33 years, with a range of 15-66 years.¹⁸ In our study, the mean age for cannabis users was 40 years for aviation fatalities, with an age range of 18-72. For all blood and urine specimens tested at CAMI, the mean age was 50 years with a range of 14-92. More than half of all fatally injured individuals tested were 50 years, or older; however, 80% of the cannabinoids users were under 50. It appears from these data that younger individuals were more likely to be using cannabis in aviation, just as in the general population. The driving population is younger than the flying population, and

would be more likely to use cannabis and be subject to impairment from the effects of high-potency cannabis. The percentage of cannabis users in motor vehicle accidents could be greater than that found in fatal aviation accidents because of the age differences between drivers and pilots, among other factors.

CONCLUSIONS

Members of the transportation industry, government regulators, and the general public should be informed of the increased potential for impairment from the use of high potency cannabis currently available and being used.

Further research should be conducted in other modes of transportation to determine the full extent of this trend and its overall impact on transportation accidents.

The typical distribution of THC-COOH in blood/urine for urine concentrations of THC-COOH above 15 ng/mL is approximately 1/10. For THC-COOH urine concentrations at or below 15 ng/mL, the blood/urine distribution was approximately 1/2.

From the data in this study, the number of potentially THC-impaired individuals involved in fatal aviation accidents increased 1.8 times from 1997 to 2006, reflecting the increased number of individuals with concentrations above the reported impairing concentration of THC in blood. Together with the other literature reports cited, this suggests that enhanced counter-measures may be warranted to reduce the use of cannabis by persons involved in transportation.

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