

Research Article



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Deltamethrin에 노출된 흰쥐의 뇨 중 3-PBA 검출 및 노출상관성

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The Correlation Between Deltamethrin Exposure and Urinary 3-PBA Concentrations in Rats

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Abstract

BACKGROUND: Pyrethroids (PYRs) are a widely used insecticide in agriculture and household area. In mammals, PYRs such as deltamethrin is metabolized to 3-phenoxybenzoic acid (3-PBA) in liver that is mainly excreted in urine. This study is designed to single exposure of deltamethrin to rats in a dose-dependent manner and identify the correlation between deltamethrin exposure and its metabolite (3-PBA) in urine.

METHODS AND RESULTS: Exposure levels of deltamethrin were control (0 mg/kg bw), low (0.0705 mg/kg bw), medium (0.705 mg/kg bw) and high (7.05 mg/kg bw) dose. Low concentration was derived by using Korea predictive operator exposure model (KoPOEM). Dermal exposure persisted for 6 h, and urine specimens were collected for 24 h. The urine matrix was removed after a series of procedures and 3-PBA was analyzed by gas chromatography/mass spectrometry.

CONCLUSION: There was a strong correlation ($R^2=0.83$) between the amount of oral exposure to deltamethrin and urinary level of 3-PBA excreted. In dermal exposure groups of deltamethrin except high-dose, also there was a good correlation between urinary 3-PBA and deltamethrin

exposure, but not stronger than in oral deltamethrin exposure groups. Based on these results, therefore, the amount of 3-PBA in urine can be used as a good monitoring indicator that reflexing the exposure level of deltamethrin to human body.

Key words: Correlation, Deltamethrin, Rats, Urinary 3-PBA

서 론

Deltamethrin [(S)-*alpha*-cyano-3-phenoxybenzyl(1*R*,3*R*)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropanecarboxylate] pyrethroids (PYRs)

. PYRs

. Deltamethrin

가 가

(Barlow *et al.*, 2001). Deltamethrin Fig. 1

Esterase ester 가

3-Phenoxybenzoic acid(3-PBA) cis-3-(2,2-Dibromovinyl)-2,2-dimethyl-cyclopropanecarboxylic acid (cis-DBCA)

(Angerer and Ritter, 1997; Arrebola *et al.*, 1999), glucuronic acid 24

(Leng *et al.*, 1997). 3-PBA PYs

cyhalothrin, cypermethrin, esfenvalerate, etofenprox, permethrin, phenothrin

3-PBA PYPs

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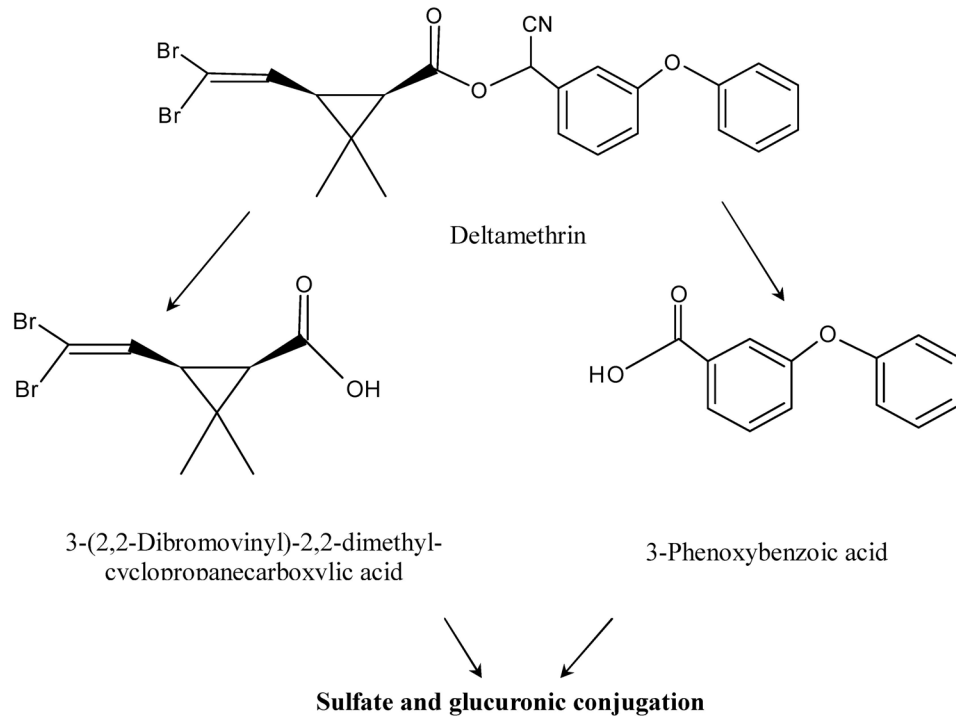


Fig. 1. Main metabolic pathways of deltamethrin in mammals.

(Wielgomas *et al.*, 2013; Watkins *et al.*, 2016; Rousis *et al.*, 2017).
 가 (Rickard *et al.*, 1985; Anadon *et al.*, 1996),
 가 .
 가 (Kim *et al.*, 2011; Hong *et al.*, 2013).

Sprague-Dawley
 ,
 deltamethrin
 3-PBA

재료 및 방법

시험물질 및 시약
 Technical deltamethrin (99.8%) Bayer
 Cropsicence (Monheim am Rhein, Germany)
 3-PBA (98%),
 2-PBA(98%), MTBSTFA
 (97%), n-hexane (95%), Toluene (99%)
 Sigma (St. Louis, MO, USA)
 creatinine Sigma (St. Louis,
 MO, USA) 1% picric acid Ricca

chemical (Arlington, TX, USA)
시험동물 및 사육조건
 Sprague-Dawley 7 (주)
 Koatech (Gyeonggi-Do, Korea) 1
 23±3°C, 50±5%, 10~15 / ,
 150~300 Lux, 12
 3

시험군의 구성 및 투여용량 설정
 ±20%
 Korea predictive operator
 exposure model (KoPOEM)
 10 , 100
 . Deltamethrin corn oil
 (7.05 mg/kg bw), (0.75 mg/kg bw)
 (0.075 mg/kg bw) 8-12
 corn oil .

투여방법
 (Zonde)
 10%
 4×4 cm

Table 1. The operating condition of GC/MS for analytes

Description	Condition
Apparatus	Agilent 6890 GC with 5973 MSD
Column	DB-5 30 m×0.32 mm×0.5 μm
Injection Temp	280°C
Injection volume	2 μL
Injection type	Splitless
Oven Temp	Initial 90°C for 1 min, 25°C/min to 120°C, 2.1°C/min to 240°C for 1.5 min, 25°C/min to 300 for 7 min

Table 2. Retention times and detected masses of the analytes

Compound	Retention time (min)	m/z
2-PBA (IS)	39.85	271, 227, 197
3-PBA	43.86	271, 227, 197

뇨 시료채취 방법

Deltamethrin
24 . 2,000 rpm 10
(Hanil, Supra 22K, Incheon, Korea)
0.45 μm
-70°C

분석기기 및 분석조건

3-PBA Agilent
(Santa Clara, CA, USA) GC (6890N)/MSD (5975)
GC-MS Table 1
Column DB-5(30 m×0.32 mm×0.5 μm)
90°C 1 , 120°C
25°C/min , 240°C 2.1°C
/min 15 , 300°C 25°C/min
7 splitless mode
2 μL selected ion
monitoring (SIM)
Table 2 3-PBA (Retention time)
Table 1 38 40

전처리 방법

Schettgen (2002)
37°C Water bath
(EYELA, SB-15, Tokyo, Japan)
1 mL (2-PBA) 10 μL (10 μg/mL),

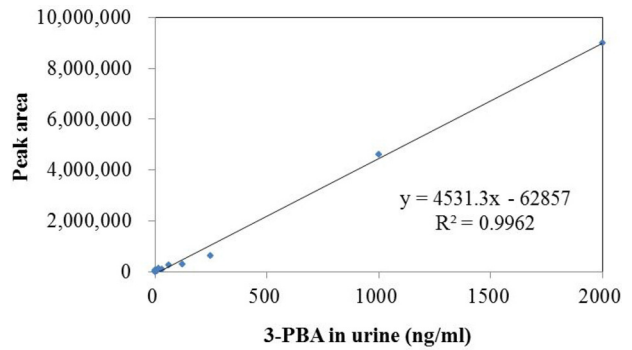


Fig. 2. Standard calibration curve of urinary 3-PBA.

HCl (12 N) 100 μL 가 oven (Vision, VS-4150ND, Daejeon-Si, Korea) 90°C, 1 가
. n-hexane 500 μL 가
10 . 1500 g 10
tube .
2 가
. Toluene 50 μL
MTBSTFA 10 μL 가
oven 70°C, 45 2 μL GC-MS

표준검정곡선 시험

3-PBA 3-PBA stock
(40 ug/mL) 0.98 ug/mL- 2.00 ng/mL
Fig. 2

뇨 중 creatinine 분석

creatinine Jaffe reaction
Ahn (2011) . 20 mg/dL
creatinine 2 7
. 96 well plate
(SPL life science, Gyeonggi-do, Korea) 20
, creatinine blank 50 μLwell⁻¹
가 creatinine reagent (1:1=0.3 N NaOH:1%
picric acid) 100 μLwell⁻¹ 가 15
Multiskan microplate
reader (Thermo Scientific, Vantaa, Finland)
480 nm 3

결과 및 고찰

뇨 중 creatinine 분석 결과

creatinine
creatinine (O'Rourke et al., 2000).
2

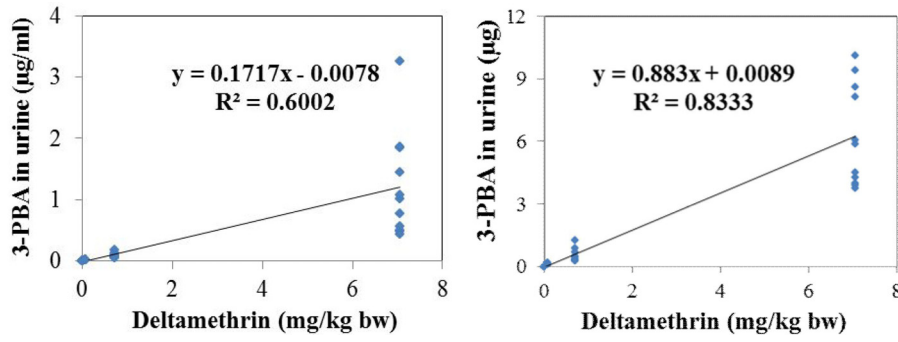


Fig. 3. The concentration ($\mu\text{g/ml}$) and amount (μg) of urinary 3-PBA in rats after single oral administration of deltamethrin.

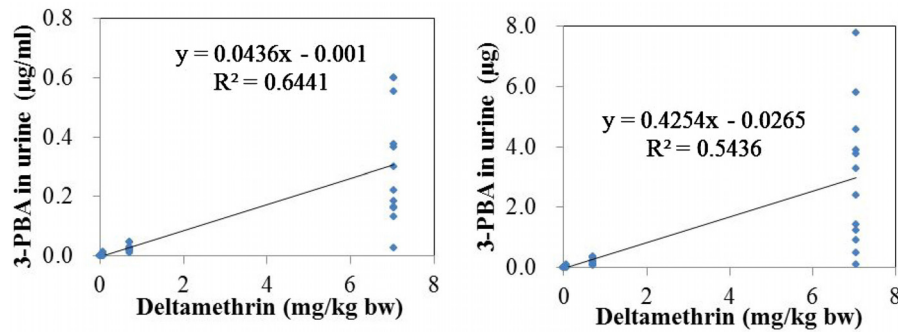


Fig. 4. The concentration ($\mu\text{g/ml}$) and amount (μg) of urinary 3-PBA in rats after single dermal administration of deltamethrin.

Table 3. Descriptive analytical data for urinary 3-PBA detected in rats

Route of administration	Groups	No. of rats	Dose (mg/kgbw)	3-PBA			
				Mean ($\mu\text{g/ml}$)	SD ($\mu\text{g/ml}$)	Mean (μg)	SD (μg)
Oral	Control	13	0	ND*	ND	ND	ND
	Low	8	0.070	0.019	0.004	0.153	0.034
	Medium	9	0.705	0.086	0.042	0.566	0.331
	High	11	7.050	1.205	0.859	6.239	2.406
Dermal	Control	8	0	ND	ND	ND	ND
	Low	10	0.070	0.004	0.005	0.026	0.029
	Medium	11	0.705	0.027	0.013	0.222	0.105
	High	12	7.050	0.307	0.193	2.977	2.328

*ND; Not Detected

Shevock (1993) , Fig. 3, Table 3
 Creatinine (R²=0.817), (R²=0.586) deltamethrin 3-PBA 3-PBA가 0.019±0.004, 0.086±0.042, 1.205±0.859 $\mu\text{g/mL}$
 (Fig. 3,4). 3-PBA Deltamethrin R²=0.600
 0.331, 6.239±2.406 μg 0.153±0.034, 0.566±
 Deltamethrin 24 (R²=0.833) deltamethrin

경피투여 후 뇨 중 3-PBA 검출

Deltamethrin
24
Fig. 4 Table 3
3-PBA가
0.004±0.005, 0.027±0.013, 0.307±0.193 µg/mL
3-PBA가 Deltamethrin
3-PBA R²=0.644
0.026±0.029,
0.222±0.105, 2.977±2.328 µg
(R²=0.5436)
3-PBA R²=0.7
Fig. 3 4 deltamethrin
3-PBA
3-PBA
R²=0.6
3-PBA R²=
0.543
deltamethrin Pharmacokinetic
modeling
가 (Godin *et al.*, 2010), 0.4-
10.0 mg/kg 18% (Kim *et al.*, 2007).
24, Rat *in vitro*
27% 70% 가
fluid , 2-4% receptor
in vivo 50%
9-24%
(Hughes and Edwards, 2010; 2016). deltamethrin
가
6
가
가
3-PBA
(Seo *et al.*, 2007; Kim *et al.*, 2015),
deltamethrin 3-PBA
3-PBA
가
가 가

Notes

The author declare no conflict of interest.

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