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2003 03 11

(71)

1555-7

(72)

1555-7

(74)

:

(54)

5-

cid)

5HTOL(5-Hydroxytryptophol) 5HIAA(5-hydroxyindoleacetic acid)

5HTOL/5HIAA

9.697 1.326 (pmol/nmol) %

16

1.017 1.821 (pmol/nmol) %

1

, , 5HTOL, 5HIAA, , .

1

2

3 1 .

4 1 .

5 2 .

6 2

7 3

8 4

9 4

10 5

11 가 1g/kg 5HTOL .

5HTOL

12 가 1g/kg
5HIAA .

5H1AA

13 5HTOL/5HIAA

14 5HTOL/5HIAA

15 5HTOL/5HIAA

cid)

5HTOL/5HIAA

9.697

1.326 (pmol/nmol) %

16

가

, ,

45000

(toxic poison)

(yeast)

(alcohol)

(ethanol)

(food), (drug)

d-altering effect)

(psychoactive drug)

1g 7.1kcal 가

'empty calories'

4kcal

(antanutrient)

(tolerance)

(narcotic)

(addictive drug)

가 (stroke), (de

mentia),

(alcoholism)

가 80% 1 (10%) 20%

(cytoplasm) NAD⁺ - (NAD⁺ - linked enzymes),
(alcohol dehydrogenase) (ADH) (acetaldehyde)
(ALDH) -CoA

(triglyceride, TG)
(membrane change) (cell necrosis)
(microsomal ethanol oxidizing system, MEOS) (drug) (foreign compounds)
MEOS MEOS가

가
가
가

ALDH 4 (isozyme) ALDH-52% ALDH- (acetaldehyde) 가
(Harada) ALDH-
ALDH-

NAD⁺ (lactate) NAD⁺
(pyruvate) 가 NAD⁺ 가
(lactate acidosis) 가
cid) (gout) pH가 가 가
(uric acid)

NADH : NAD 가 N
(oxaloacetate)
ADH : NAD (malate)
(phosphoenol pyruvate)
(gluconeogenesis) 가 (hypoglycemia)
cemia) 가 (hyperosmolarity),
1kg 1g
e Na⁺, K⁺ -ATPase
(macromolecules) 가
가
가
80% (macrovesicular fat droplet)
(fatty liver) 가
가
가
GSH 10 가 GSH
(cysteine) GSH
E 가 GSH
(peptidylproline hydroxylase) 가 가
(endorphin)
(serotonin) (5-hydroxytryptamine, 5HT) (enterochromaffin cell)
(tryptophan) 5- 가
ATP (neurotransmitter)
5HIAA (5-hydroxyindoleacetic acid)

(affective psychosis) (rapheal nuclei)

(epinephrine) 가

(carcinoid syndrome) (bradykinin)

(neurotransmitter) 가 (norepinephrine), (synapse) (dopamine)

(chronic syndrom) 가

1961 (Schain) (Freeman)

23 1976 (Goldstein) 72 6

1981 (Young)

33%가

(5-hydroxytryptamine) MAO(monoamin oxidase)

5HIAL(5-hydroxyindole - 3 - acetaldehyde) (oxidative deamination)

ALDH(aldehyde dehydrogenase) 5HIAA(5-hydroxyindole - 3 - acetic acid) , ADH(

alcohol dehyddrogenase) 5HTOL(5-hydroxy - tryptophol) .(1)

5HIAA , 5HTOL 5HIAA

1% 5HTOL sulfuric acid glucuronic acid UDP(urine di

phosphate) - (glucuronosyl - transferase) (phenol sulfotransf

erase)가 (conjugation) (conjugation)

(detoxification processes) . 5HTOL UDPGA(urine diphosphoglucuronic acid)

(glucuronide conjugates) (microsomal) UDP

- (glucuronosyltransferase)가 . 5HTOL (sulfoconjugation) P

APS(3' - phosphoadenosine - 5' - phosphosulfate)

가 5HTOL (sulfuric acid)

17%

가

5HTOL

ALDH 5HIAA 5HTOL 가 5-HT가

(, , ,)

(biogenic amines) (5HT, 5

hydroxytryptophol) 5HIAL 5HIAA 5HTOL

NADH/NAD+ 가 5HTOL ADH ALDH

(re-oxidation)

5HTOL/5HIAA

가

(Hagan) (Hela

11 11-16 5HTOL/5HIAA

pmol/nmol% Kg 0.6g 5HTOL 가

가 (biomarker)

<2차 임상실험>

		알콜 섭취								
시간	0	0.5	1	1.5	2	2.5	3	3.5	4	
호기		○	○	○	○	○	○			
혈액			◎		◎		◎			

<3>

<3차 임상실험>

		알콜 섭취																		
시간	0	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5	5.5	6							
호기	○	○	○	○	○	○	○													
혈액	◎	◎	◎	◎	◎	◎	◎													

<4>

<4차 임상실험>

		알콜																		
시간	0	2	4	6	8	10	12	14	16	18	20	22	24							
호기	○	○	○	○	○															
혈액	◎	◎	◎	◎	◎															
노	●	●	●	●	●		●		●		●		●							

2:

2 3 1 1 (360ml) , 4 (5 22%) 1½ (540ml) 1g/kg ,

3:

2 90 22% 540ml/person, 360ml/person , 1g/kg 1 (,) (Lion Alcoholmeter SD-400) ,

4:

가 catheter 2ml hepar inized cap . Heparinized vacutainer tube 3,000rpm 20 .

5:

(0, 2, 4, 6, 8, 12, 16, 20, 24 hrs) 4 12,000 rpm -70 .

6:

D-400) (30, 60, 90, 120, 150, 180, 210, 240) (Lion Alcolmeter S

7:

6.25%(w/v) 1.8ml (ethanol assay kit) (SIGIMA 332-B) 0.2ml
(trichloroacetic acid) 2,000rpm 5
10ul 3ml NAD-ADH 10
340nm 10

8: 5-HTOL 5-HIAA

(internal standard) 4 (HPLC-EC) 5-HTOL 5-HIAA
(1mM disodium EDTA 1mM (sodium octanesul
fonic acid) 0.1M (monobasic sodium phosphate) (pH 4.0
) 7:3 20μℓ HPLC
(Milford, MA) HPLC(elctrochemical detector, model 460) 5μm, 4.6mm×15cm C18 (Young-in pak;Gins
co), column inlet filter(type 73xx;Rheodyne, Corati, Calif.) Ag/AgCl
0.55 V 0.1M monobasic sodium phosphate/10%acetonitrile(1mM disodium EDTA, 1
mM sodium actane-sulfonic acid) pH 4.0 1ml/min
5-HTOL 5-HTOL/DHBA
SAS (SAS institute, 1990)
ANOVA

8:

<1 >

1 16 (male = 7, female = 9) 20-27 22 ± 1.8 , 1
67 ± 7.3cm, 62.8 ± 11/4 Kg, BMI 22.5 ± 3 . (1)

1. Anthropometric measurements of the subject

Anthropometric measurements of the subject

		Control Group	Alcohol Group
1'st	Age (yrs)	21.0 ± 2.1	22.0 ± 0.9
	High (cm)	166 ± 9.6	164.3 ± 8.1
	Weight(Kg)	70.6 ± 16.2	55.6 ± 8.1
	BMI	25.3 ± 2.1	22.6 ± 10.2
2'st	Age (yrs)	23.6 ± 1.2	23.0 ± 2.2
	High (cm)	170.0 ± 3.5	174.5 ± 5.0
	Weight(Kg)	61.1 ± 1.6	66.8 ± 12.6
	BMI	21.1 ± 0.5	21.9 ± 3.7
3'rd	Age (yrs)	22.3 ± 2.1	21.6 ± 1.5
	High (cm)	166.5 ± 7.1	170.7 ± 6.3
	Weight(Kg)	72.2 ± 17.7	59.7 ± 3.4
	BMI	22.3 ± 2.1	21.6 ± 1.5
4'th	Age (yrs)	24.0 ± 2.8	23.0 ± 1.7
	High (cm)	171.9 ± 4.6	174.8 ± 6.4
	Weight(Kg)	68.6 ± 10.2	74.2 ± 6.8
	BMI	105.9 ± 14.7	110.2 ± 4.9

20, 40, 60 (non-diet alcohol group, NDAG) 2 3
0.086 ± 0.01%(w/v) 20
40 60 0.068 ± 0.005%(w/v)
가 가

2. Alcohol Concentration in Respiration (1)

Alcohol Concentration in Respiration (1차 임상실험)		
Time (min)	Alcohol, %(v/w)	
	Control Group	Alcohol Group
20	0.0±0.0	0.068±0.005
40	0.0±0.0	0.123±0.013
60	0.0±0.0	0.182±0.022

Values are mean±SEM, n=5.

3 4 . 10 Empty
8.766 ± 1.426 (mg/dl), 7.621 ± 1.302 (mg/dl)
60 49.079 ± 8.441 (mg/dl) 35.914 ± 1.166 (mg/dl) .

3. Alcohol Concentration in Blood (1)

Alcohol Concentration in Blood (1차 임상실험)		
Time (min)	Alcohol, (mg/dl)	
	Control G.	Alcohol G.
10	8.766±1.426	7.621±1.302
60	49.079±8.441	35.914±1.166

Values are mean±SEM, n=5.

(Shuamte) 30 60 - 90 %가
60 95%, 90 100% 60-90
, non-diet , 360ml 50
가 가 180ml 가 60
가 .
<2 >
2 20 (male = 16, female = 4) 23 ± 1.6 , 171 ± 4.5 cm,
65.6 ± 8.8 Kg, BMI 22.3 ± 2.6 . (1)
1 1 가 2
540ml 360ml . 2
4 5 , 30 0.103 ± 0.001 %(w/v) , 60
0.134 ± 0.019%(w/v) . 3
0.083 ± 0.003 %(w/v) (0.050 - 0.099 %w/v)

4. Alcohol Concentration in Respiration (2)

Alcohol Concentration in Respiration (2차 임상실험)

Time (hrs)	Alcohol, %(v/w)	
	Control G.	Alcohol G.
30	0.0±0.0	0.103±0.001
60	0.0±0.0	0.134±0.019
90	0.0±0.0	0.111±0.010
120	0.0±0.0	0.105±0.005
150	0.0±0.0	0.097±0.004
180	0.0±0.0	0.083±0.003

Values are mean±SEM, n=5.

60-90
가
5 6
120 (27.393 ± 2.516 mg/dl)
60 , 120 , 180 3 1 60
60

5. Alcohol Concentration in Blood (2)

Alcohol Concentration in Blood (2차 임상실험)

Time (min)	Alcohol, (mg/dl)	
	Control G.	Alcohol G.
60	8.215±0.0033	24.177±1.359
120	7.803±0.0090	27.383±2.516
180	8.1395±0.0012	24.843±1.583

s are mean±SEM, n=5.

<3 >

3 11 (male = 8, female = 3) 21.3 ± 1.9 , 172.5 ± 5.7 cm,
66.7 ± 9.2 Kg, BMI 22.5 ± 3.2 . (1)
2 , 30 30 3
0.084 ± 0.007%(w/v) 6 7 . 30
, 60 0.117 ± 0.001 %(w/v)
90 0.133 ±0.001 %(w/v)
. 2 가 60 3
90 , 3
0.081 ±0.001 %(w/v) %(w/v)
가 3 2 .

6. Alcohol Concentration in Respiration (3)

Alcohol Concentration in Respiration (3차 임상실험)

Time (hrs)	Alcohol, %(w/v)	
	Control G.	Alcohol G.
30	0.0±0.0	0.084±0.007
60	0.0±0.0	0.117±0.001
90	0.0±0.0	0.133±0.001
120	0.0±0.0	0.112±0.001
150	0.0±0.0	0.100±0.005
180	0.0±0.0	0.081±0.001

Values are mean±SEM, n=5.

<4 >

4 16 (male = 16) 24.5 ± 2.2 , 173.4 ± 5.5 cm, 71
.4 ± 8.5 Kg, BMI 23.7 ± 2.2 . (1). 2 3 360ml/person
1g/kg
4 1, 2, 4, 6 8 , 2 3 3 4

7	8	1	0.1036 ± 0.033 %(w/v)	4
	0.0574 ± 0.025 %(w/v)			6
	0.366 ± 0.019 %(w/v)	8	가	0.0126 ± 0.012 %(w/v)

7. Alcohol Concentration in Respiration (4)

Time (hrs)	Alcohol, %(w/v)	
	Control G.	Alcohol G.
0	0.0±0.0	0.0±0.0
1	0.0±0.0	0.1036±0.033
2	0.0±0.0	0.0921±0.029
4	0.0±0.0	0.0574±0.025
6	0.0±0.0	0.0366±0.019
8	0.0±0.0	0.0126±0.012

Values are mean $\pm$ SD, n=5.

0.0011 ± 0.0016	0.0081 ± 0.0033 % (w/v)	
2	0.1307 ± 0.0622 % (w/v)	8
0.0123 ± 0.0193 % (w/v)	.	

8. Alcohol Concentration in Blood (4)

Time (hrs)	Alcohol, %(w/v)	
	Control G.	Alcohol G.
0	0.0038±0.0037	0.0006±0.0017
2	0.0081±0.0033	0.1307±0.0622
4	0.0013±0.0017	0.0961±0.0197
6	0.0011±0.0016	0.0475±0.0222
8	0.0033±0.0038	0.0123±0.0193

Values are mean $\pm$ SD, n=5.

<5 >

1-4	9	10	5
가	1	0.0923 ± 0.0296 % (w/v)	0.0483 ± 0.0068 % (w/v)
1	4	0.182 ± 0.022 % (w/v), 2	0.134 ± 0.019 % (w/v), 3
001 % (w/v), 4	0.1036 ± 0.033 % (w/v)		0.133 ± 0.001 % (w/v), 4
		ADH (alcohol dehydrogenase)	ALDH (aldehyde dehydrogenase)
		MEOS (microsomal ethanol oxidizing system)	

9. Alcohol Concentration in Respiration (5)

Alcohol Concentration in Respiration (5차 임상실험)

Time (hrs)	Alcohol, %(w/v)	
	Control G.	Alcohol G.
0	0.0±0.0	0.0±0.0
1	0.0±0.0	0.0923±0.0236
2	0.0±0.0	0.0793±0.0040
3	0.0±0.0	0.0627±0.0072
4	0.0±0.0	0.0483±0.0068

Values are mean±SD, n=5.

1-5, 1, 30, 2, 1, 1, 30

4, 6

9: 5HIAA 5HTOL

가 1g/kg 1 (0, 2, 4, 6, 8, 12, 16, 2

4) 10-13 11-15

5HIAA (5-hydroxyindole acetic acid) 5HTOL (5-hydroxytryptophol)

5HTOL 11 5HTOL 가

6 28.0664pmol 16 1.2694p

mol 2.4515pmol 5HIAA 11 12

ogenic amines) 4-8 (5HT, 5hydroxy- tryptophol) (bi

5HIAL 5HIAA 5HTOL

ratio 가 5HTOL ADH acetaldehyde ALDH (re-oxidation) NADH/NAD+

5HIAA 5HTOL 5HTOL/5

HIAA ratio

10. The 5HTOL concentration in urine

The 5HTOL concentration in urine.

Time (hrs)	5HTOL concentration (pmol)	
	Control G.	Alcohol G.
0	1.8561	2.3203
2	1.5731	3.3450
4	1.7270	5.7440
6	4.3822	28.0964
8	1.7271	7.9276
12	1.0941	7.8389
16	1.3649	2.4315
24	1.9006	-

11. The 5HIAA concentration in urine

The 5HIAA concentration in urine.

Time (hrs)	5HIAA concentration (nmol)	
	Control G.	Alcohol G.
0	0.0269	0.0257
2	0.0282	0.0203
4	0.0157	0.0110
6	0.0364	0.0267
8	0.0330	0.0264
12	0.0347	0.0340
16	0.0313	0.0328
24	0.0278	-

12. The 5HTOL/5HIAA ratio in urine

The 5HTOL/5HIAA ratio in urine.

Time (hrs)	5HTOL/5HIAA ratio (pmol/nmol)%	
	Control G.	Alcohol G.
0	1.682	1.691
2	1.821	2.884
4	1.172	6.652
6	1.389	9.697
8	1.140	5.5
12	1.017	2.901
16	1.077	1.326
24	1.543	-

13. The 5HTOL/5HIAA ratio (pmol/nmol) in urine

The 5HTOL/5HIAA ratio (pmol/nmol) in urine.

Time (hrs)	5HTOL/5HIAA(pmol/nmol)	
	Control G.	Alcohol G.
0	103.20	189.10
2	182.10	256.40
4	117.20	665.19
6	138.90	969.71
8	114.00	550.26
12	101.70	290.06
16	107.70	132.26
24	154.31	-

10: 5HTOL/5HIAA (pmol/nmol) ratio

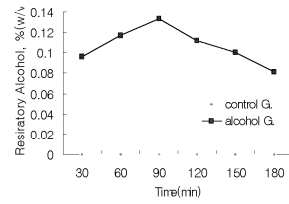
(5HT) (tryptophan) .(1) (5HT)
(monoamine oxidase) (5HIAL)
(aldehyde dehydrogenase) 5HIAL 5HIAA(5-hydroxyindol-3-acetic acid)
, 5HIAA (alcohol dehydrogenase)
(aldehyde reductase) 5HIAL 5HIAA

5HTOL/5HIAA ratio 12-13 13-15
, 5HTOL/5HIAA 1.017 - 1.821 (pmol/nmol)% 1.
27 % , 6 9.69 %
16 1.326 %
1.27 %

5HTOL/5HIAA ratio 가
5HIAA 1% 가
5-HTOL 1.5 % cutoff 가
4 6
15-16 가 가
가

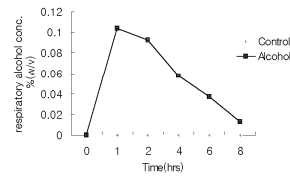
7

Alcohol Concentration in Respiration (3차 임상실험)



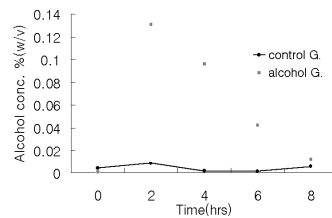
8

Alcohol Concentration in Respiration (4차 임상실험)



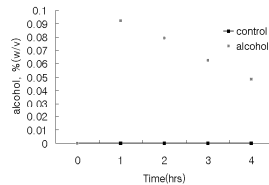
9

Alcohol Concentration in Blood (4차 임상실험)



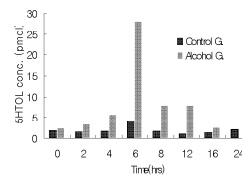
10

Alcohol Concentration in Respiration (5차 임상실험)



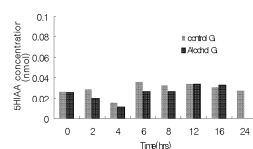
11

Time-course of the urinary 5HTOL concentration (mean values) after healthy volunteers ingested 1g/kg ethanol



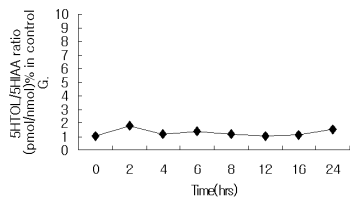
12

Time-course of the urinary 5HIAA concentration (mean values) after healthy volunteers ingested 1g/kg ethanol



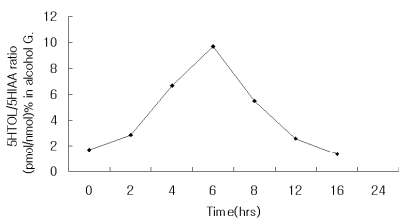
13

The 5HTOL/5HIAA ratio in urine from non alcohol group



14

The 5HTOL/5HIAA ratio in urine from alcohol group



15

Time-course of the 5HTOL/5HIAA ratio after healthy volunteers ingested 5g/kg ethanol

