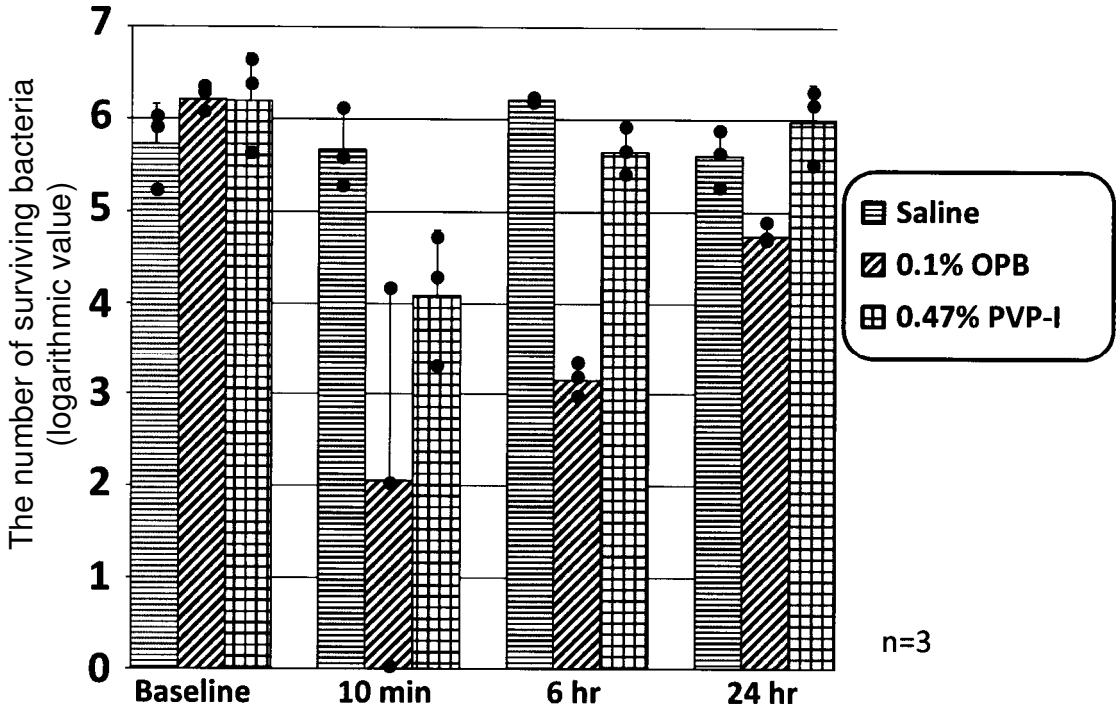
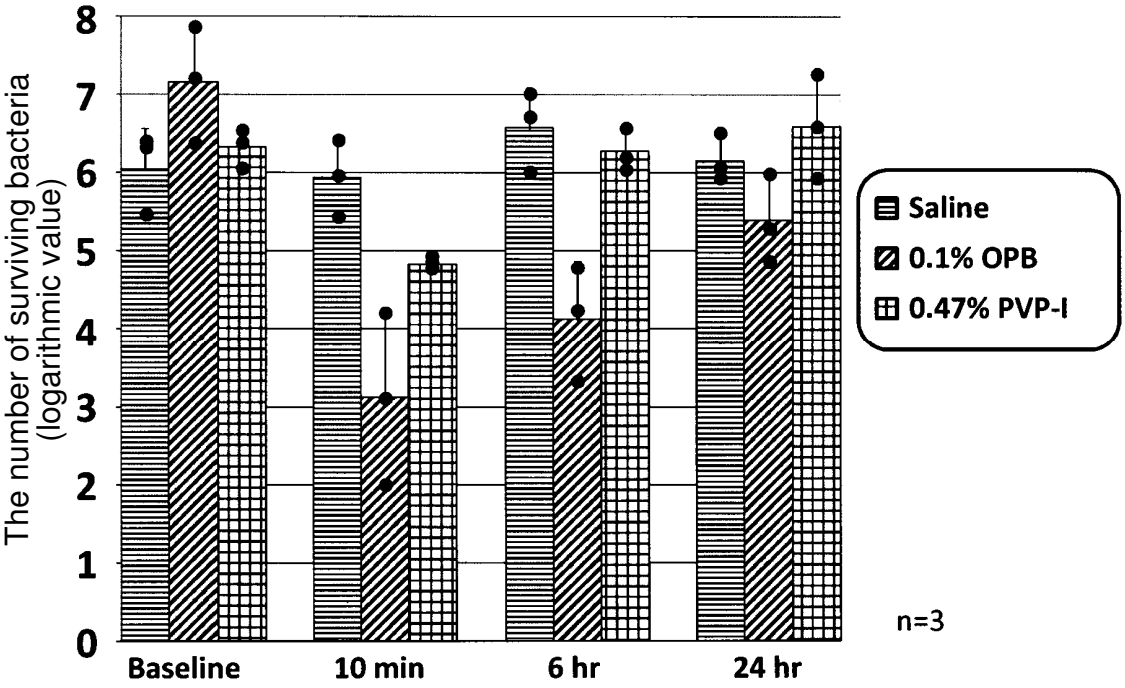
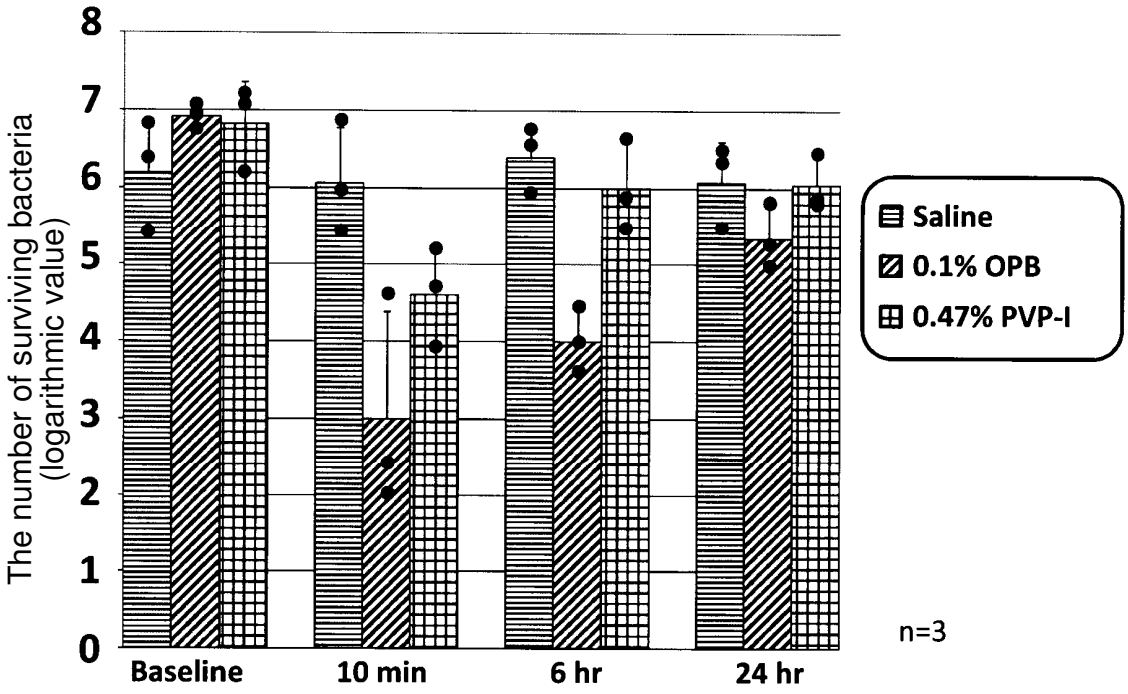
[Fig. 1]


The number of surviving bacteria
(logarithmic value)
0
1
2
3
4
5
6
7
Baseline
10 min
6 hr
24 hr
Saline
0.1% OPB
0.47% PVP-I
n=3

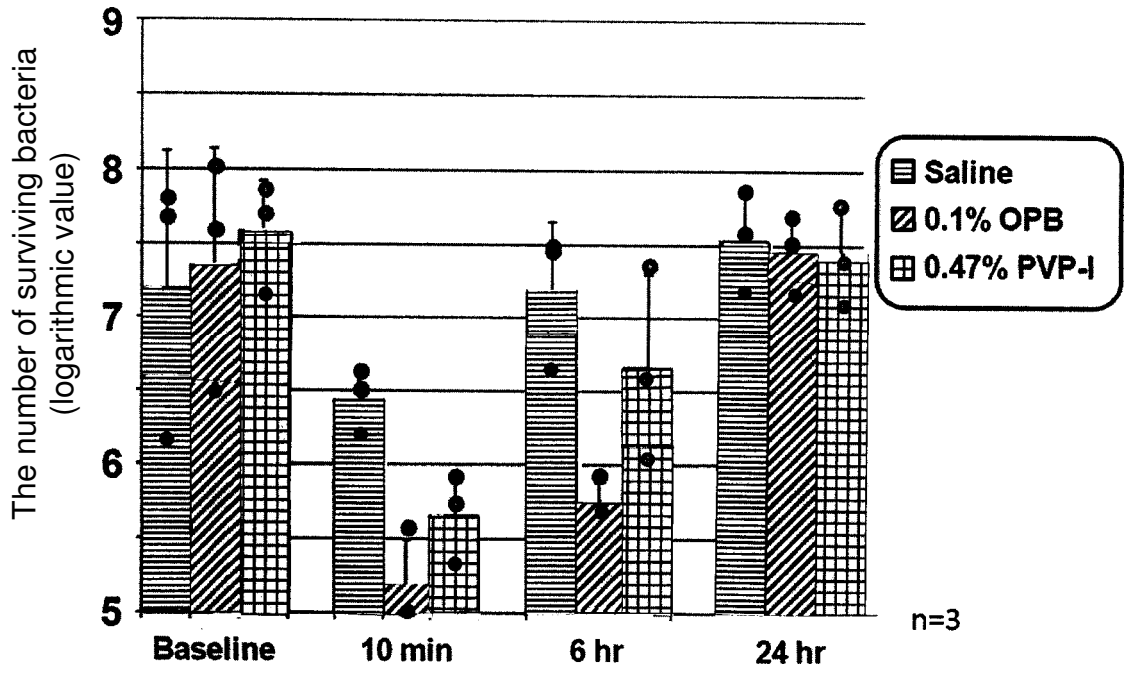
[Fig. 2]


The number of surviving bacteria
(logarithmic value)
0
1
2
3
4
5
6
7
8
Baseline
10 min
6 hr
24 hr
Saline
0.1% OPB
0.47% PVP-I
n=3

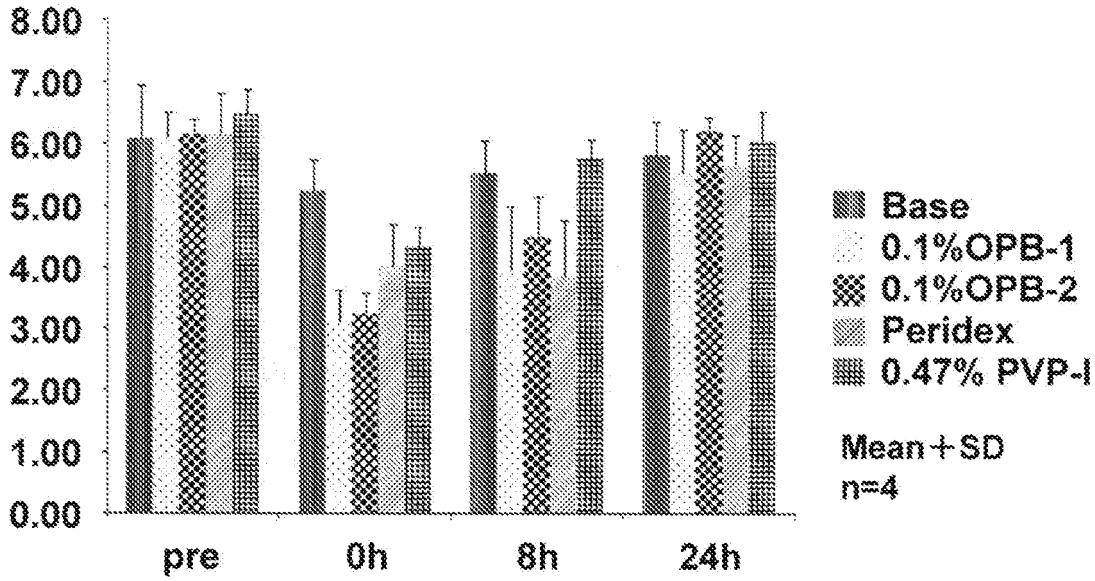
[Fig. 3]


The number of surviving bacteria
(logarithmic value)
0
1
2
3
4
5
6
7
8
Baseline
10 min
6 hr
24 hr
Saline
0.1% OPB
0.47% PVP-I
n=3

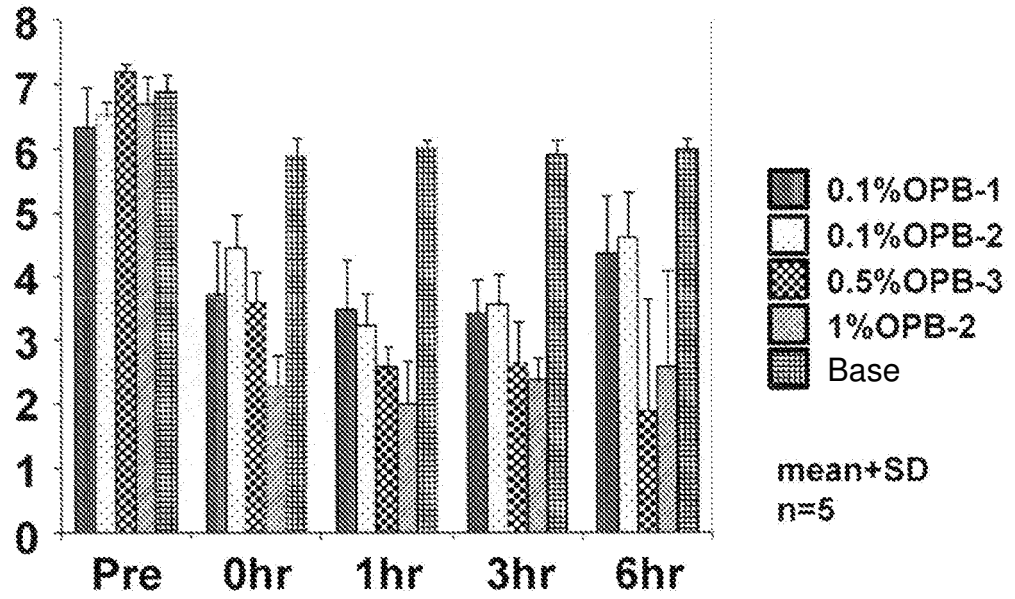
[Fig. 4]


The number of surviving bacteria
(logarithmic value)
5
6
7
8
9
Baseline
10 min
6 hr
24 hr
Saline
0.1% OPB
0.47% PVP-I
n=3

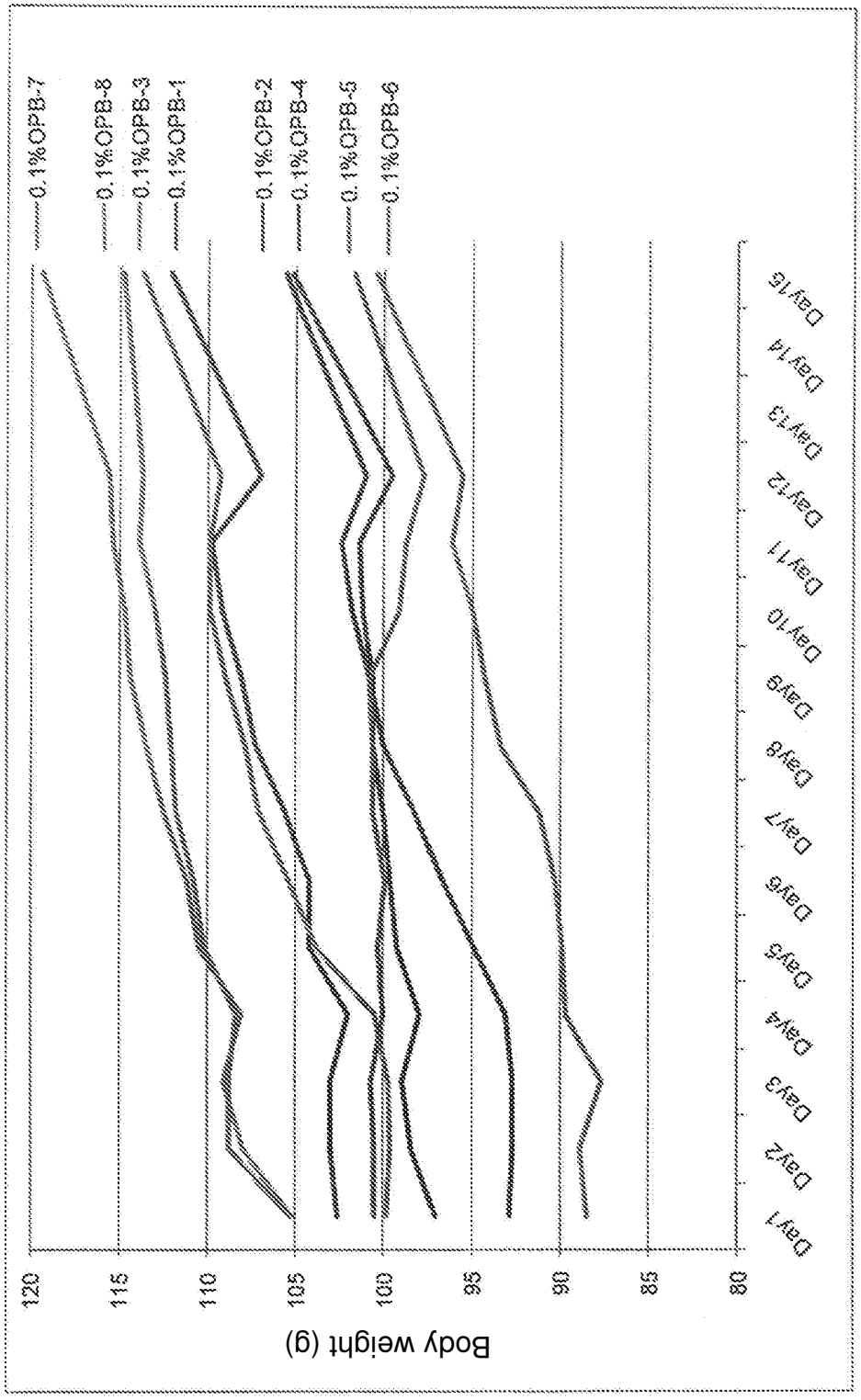
[Fig. 5]


8.00
7.00
6.00
5.00
4.00
3.00
2.00
1.00
0.00
pre
0h
8h
24h
Base
0.1%OPB-1
0.1%OPB-2
Peridex
0.47% PVP-I
Mean+SD
n=4

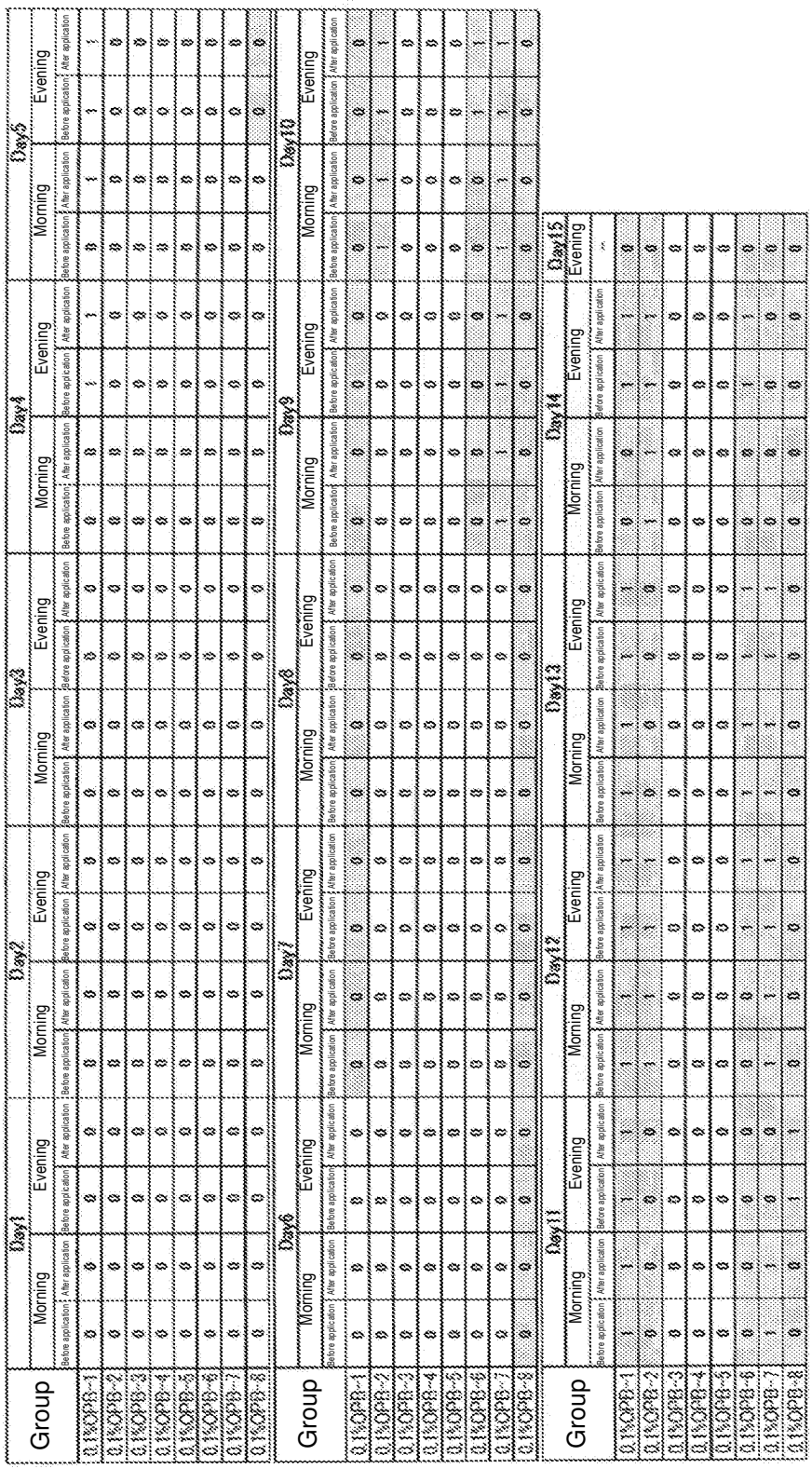
[Fig. 6]


8
7
6
5
4
3
2
1
0
Pre
0hr
1hr
3hr
6hr
0.1%OPB-1
0.1%OPB-2
0.5%OPB-3
1%OPB-2
Base
mean+SD
n=5

[Fig. 7]


Body weight (g)
120
115
110
105
100
95
90
85
80
Day1
Day2
Day3
Day4
Day5
Day6
Day7
Day8
Day9
Day10
Day11
Day12
Day13
Day14
Day15
0.1%OPB-7
0.1%OPB-8
0.1%OPB-3
0.1%OPB-1
0.1%OPB-2
0.1%OPB-4
0.1%OPB-5
0.1%OPB-6

[Fig. 8]



Group	Day1				Day2				Day3				Day4				Day5			
	Morning		Evening		Morning		Evening		Morning		Evening		Morning		Evening		Morning		Evening	
	Before application	After application	Before application	After application	Before application	After application	Before application	After application	Before application	After application	Before application	After application	Before application	After application	Before application	After application	Before application	After application	Before application	After application
0.1%OPB-1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1
0.1%OPB-2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.1%OPB-3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.1%OPB-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.1%OPB-5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.1%OPB-6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.1%OPB-7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.1%OPB-8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Group	Day6				Day7				Day8				Day9				Day10			
	Morning		Evening		Morning		Evening		Morning		Evening		Morning		Evening		Morning		Evening	
	Before application	After application	Before application	After application	Before application	After application	Before application	After application	Before application	After application	Before application	After application	Before application	After application	Before application	After application	Before application	After application	Before application	After application
0.1%OPB-1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.1%OPB-2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1
0.1%OPB-3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.1%OPB-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.1%OPB-5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.1%OPB-6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.1%OPB-7	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1
0.1%OPB-8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Group	Day11				Day12				Day13				Day14				Day15			
	Morning		Evening		Morning		Evening		Morning		Evening		Morning		Evening		Morning		Evening	
	Before application	After application	Before application	After application	Before application	After application	Before application	After application	Before application	After application	Before application	After application	Before application	After application	Before application	After application	Before application	After application	Before application	After application
0.1%OPB-1	1	1	1	1	1	1	1	1	1	1	1	1	0	0	1	1	0	0	-	-
0.1%OPB-2	0	0	0	0	1	1	1	1	0	0	0	0	1	1	1	1	0	0		
0.1%OPB-3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
0.1%OPB-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
0.1%OPB-5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
0.1%OPB-6	0	0	0	0	0	0	1	1	1	1	1	1	0	0	1	1	0	0		
0.1%OPB-7	1	1	0	0	1	1	1	1	1	1	1	1	0	0	0	0	0	0		
0.1%OPB-8	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0		

[Fig. 9A]

Photo 1 0.1%OPB-1 group

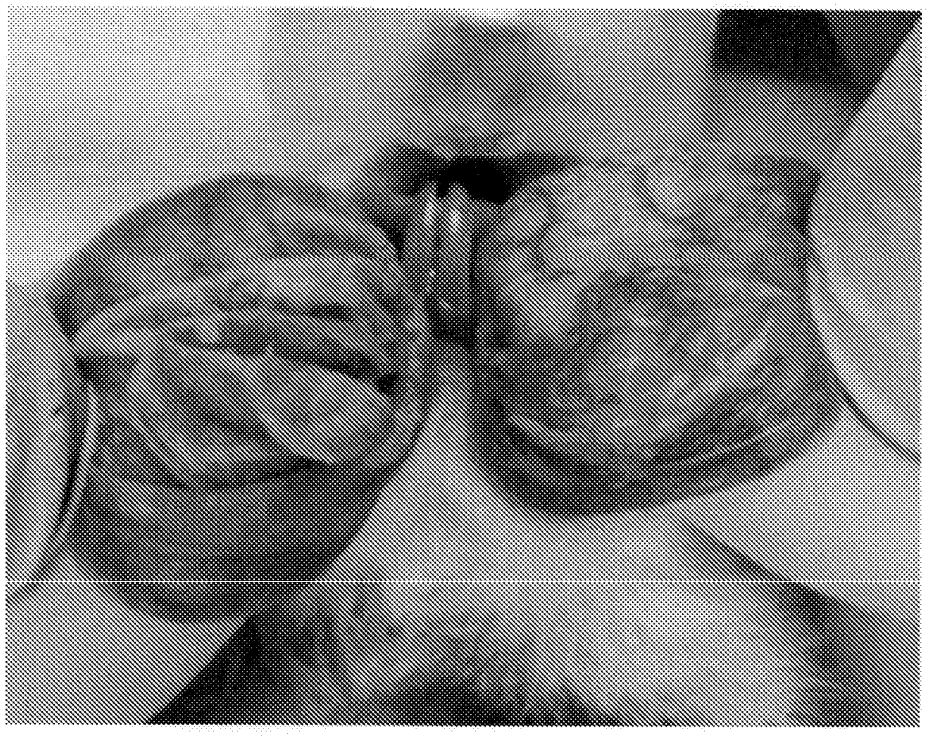


Photo 2 0.1%OPB-2 group



[Fig. 9B]

Photo 3 0.1%OPB-3 group

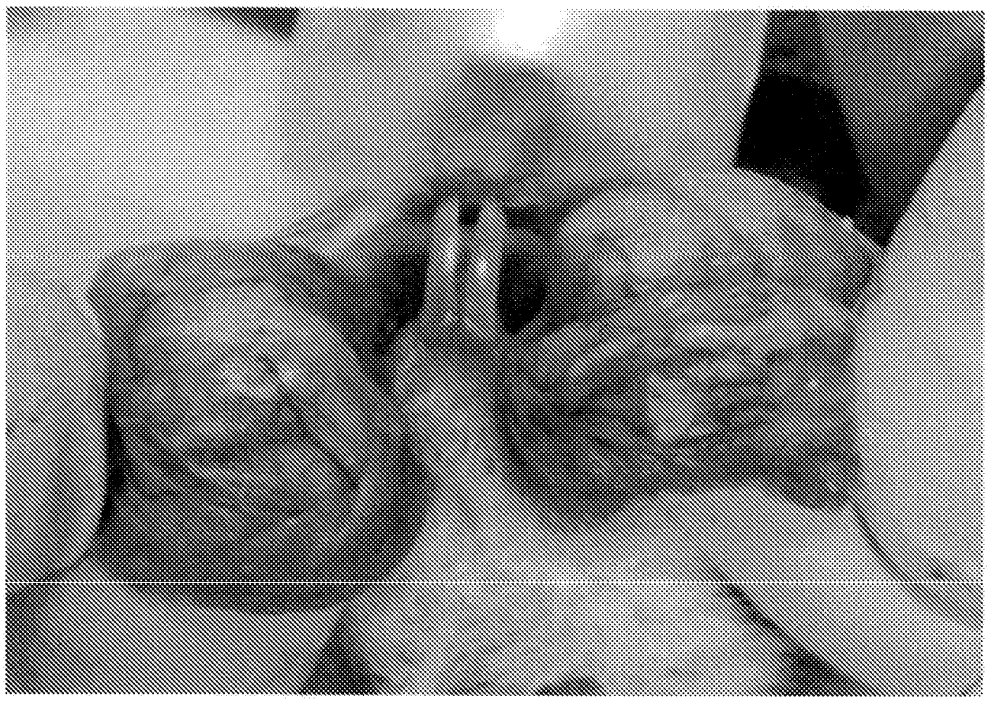


Photo 4 0.1%OPB-4 group



[Fig. 9C]

Photo 5 0.1%OPB-5 group

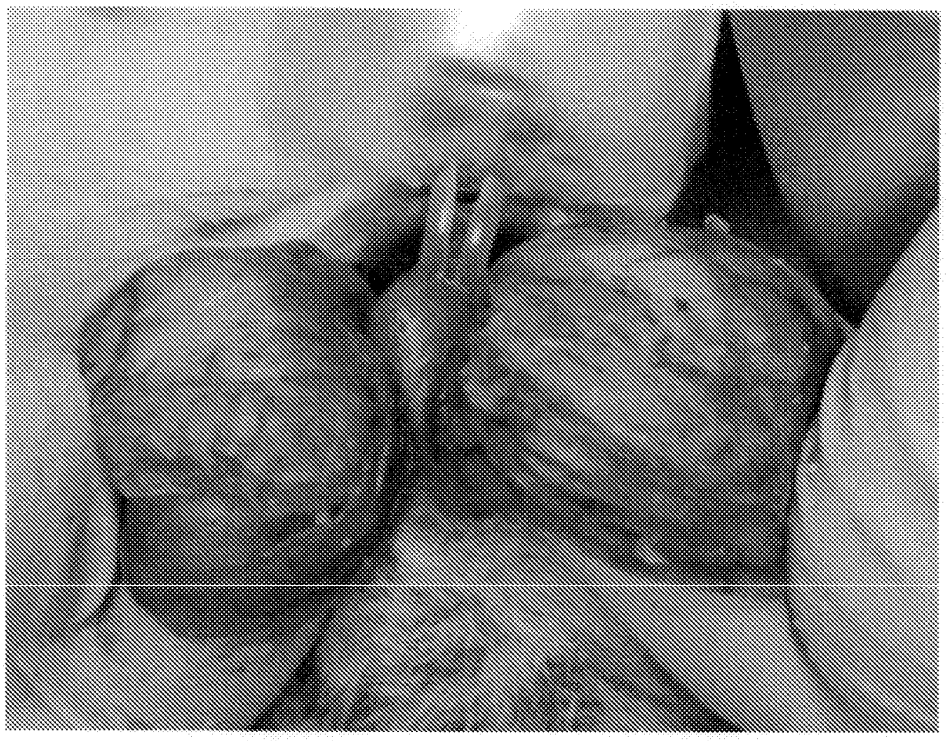
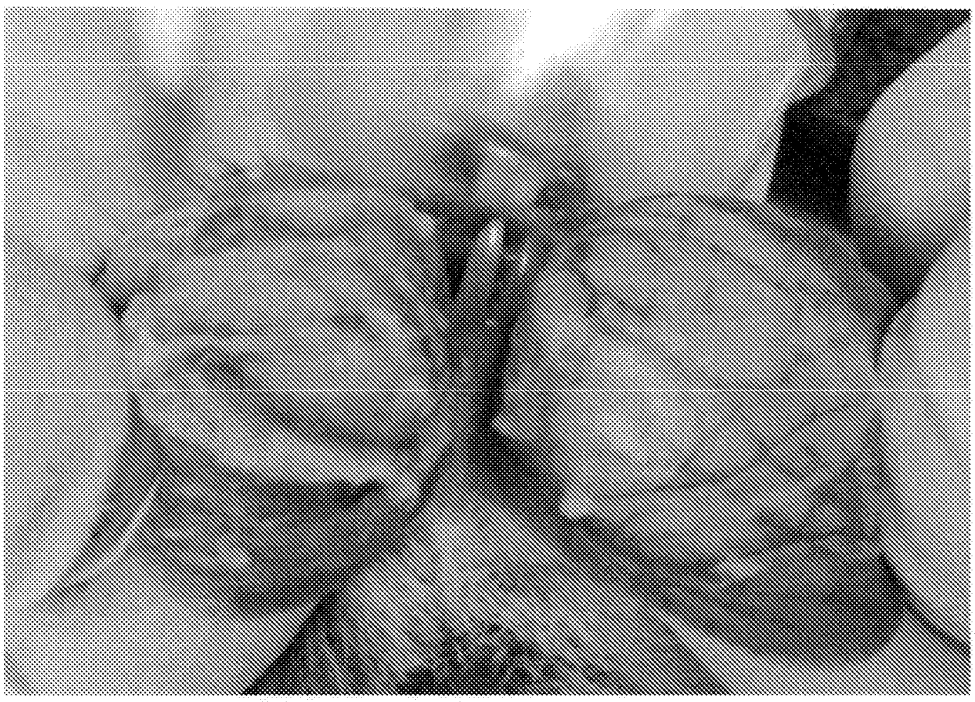


Photo 6 0.1%OPB-6 group



[Fig. 9D]

Photo 7 0.1%OPB-7 group



Photo 8 0.1%OPB-8 group



[Fig. 10]

Organ:	Group	0.1% OPB-1			0.1% OPB-2			0.1% OPB-3			0.1% OPB-4			0.1% OPB-5		
Histopathological manifestation	Animal No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
	Sample No.	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30
Right cheek pouch, oral mucosa																
Epithelium (cell degeneration, metaplasia, or erosion)		0	0	1	0	1	1	0	0	0	0	1	0	0	1	1
Leukocyte infiltration		2	1	2	1	3	1	0	0	0	0	2	0	0	1	1
Vascular congestion		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Edema		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Inflammation index		2	1	3	1	4	2	0	0	0	0	3	0	0	2	2
Average grade		2			2			0			1			1		
Other manifestations																
Intercellular edema		-	-	±	-	±	-	-	-	-	-	-	-	-	-	-
Increased keratosis		+	+	+	+	+†	+	-	-	-	±	±	±	±	±	±

Grade in other manifestations: −: within normal limited, ±: very slight, +: slight, 2+: moderate, 3+:severe

†: parakeratotic

Organ:	Group	0.1% OPB-6			0.1% OPB-7			0.1% OPB-8		
	Animal No.	16	17	18	19	20	21	22	23	24
Histopathological manifestation	Sample No.	32	34	36	38	40	42	44	46	48
Right cheek pouch, oral mucosa										
Epithelium (cell degeneration, metaplasia, or erosion)		1	1	1	1	1	1	1	1	1
Leukocyte infiltration		1	1	2	1	1	2	3	2	2
Vascular congestion		0	0	0	0	0	0	0	0	0
Edema		0	0	0	0	0	0	0	0	0
Inflammation index		2	2	3	2	2	3	4	3	3
Average grade		2			2			3		
Other manifestations										
Intercellular edema		-	-	-	-	-	-	±	-	-
Increased keratosis		+	+	+	+	+†	+	+	+	+

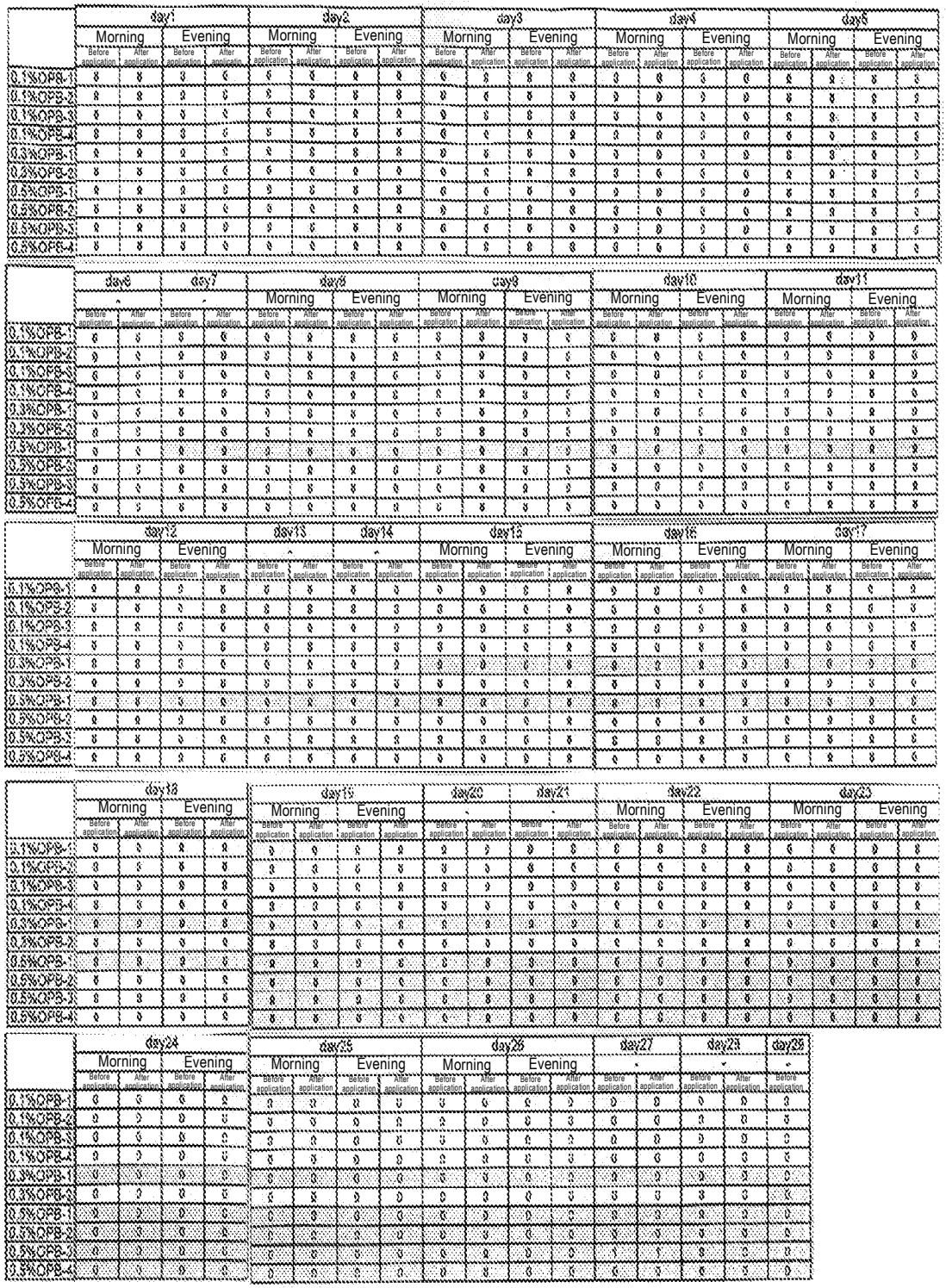
Grade in other manifestations: −: within normal limited, ±: very slight, +: slight, 2+: moderate, 3+:severe

†: parakeratotic

Organ:	Group	Control(DW)																							
Histopathological manifestation	Animal No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
	Sample No.	1	3	5	7	9	11	13	15	17	19	21	23	25	27	29	31	33	35	37	39	41	43	45	47
Right cheek pouch, oral mucosa		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Epithelium (cell degeneration, metaplasia, or erosion)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1	0	0	0	0	0	0	0	2
Leukocyte infiltration		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Vascular congestion		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Edema		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Inflammation index		0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1	0	0	0	0	0	0	0	2
Average grade														0											
Other manifestations																									
Intercellular edema		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Increased keratosis		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Grade in other manifestations: −: within normal limited, ±: very slight, +: slight, 2+: moderate, 3+:severe

[Fig. 11]



[Fig. 12]

Organ:	Group	0.1% OPB-1			0.1% OPB-2			0.1% OPB-3			0.1% OPB-4			0.3% OPB-1			0.3% OPB-2		
Histopathological manifestation	Animal No.	1	2	3	4	5	6	7	8	9	10	11	12	19	20	21	22	23	24
	Sample No.	1L	2L	3L	4L	5L	6L	7L	8L	9L	10L	11L	12L	19L	20L	21L	22L	23L	24L
Right cheek pouch, oral mucosa																			
Epithelium (cell degeneration, metaplasia, or erosion)		0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	0
Leukocyte infiltration		0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0
Vascular congestion		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Edema		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Inflammation index		0	0	0	0	0	0	0	0	0	0	0	0	2	2	2	1	1	0
Average grade			0			0			0			0			2			1	
Other manifestations																			
Intercellular edema		±	−	−	±	−	±	−	+	−	−	−	±	+	+	2+	+	+	+
Increased keratosis		−	−	−	−	−	−	−	−	−	−	−	−	−	±	±	−	−	−
Intraepidermal microabscess		−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−

Grade in other manifestations: −: within normal limited, ±: very slight, +: slight, 2+: moderate, 3+:severe

Organ:	Group	0.5% OPB-1			0.5% OPB-2			0.5% OPB-3			0.5% OPB-4		
Histopathological manifestation	Animal No.	31	32	33	34	35	36	37	38	39	40	41	42
	Sample No.	31L	32L	33L	34L	35L	36L	37L	38L	39L	40L	41L	42L
Right cheek pouch, oral mucosa													
Epithelium (cell degeneration, metaplasia, or erosion)		1	1	1	1	1	1	1	1	1	0	1	1
Leukocyte infiltration		2	1	2	0	0	0	1	1	1	0	1	1
Vascular congestion		0	0	0	0	0	0	0	0	0	0	0	0
Edema		0	0	0	0	0	0	0	0	0	0	0	0
Inflammation index		3	2	3	1	1	1	2	2	2	0	2	2
Average grade			3			1			2			1	
Other manifestations													
Intercellular edema		2+	2+	2+	2+	+	±	2+	2+	2+	+	2+	2+
Increased keratosis		±	±	±	−	−	−	−	±	±	−	−	±
Intraepidermal microabscess		−	−	−	−	−	−	−	−	−	−	−	−

Grade in other manifestations: −: within normal limited, ±: very slight, +: slight, 2+: moderate, 3+:severe

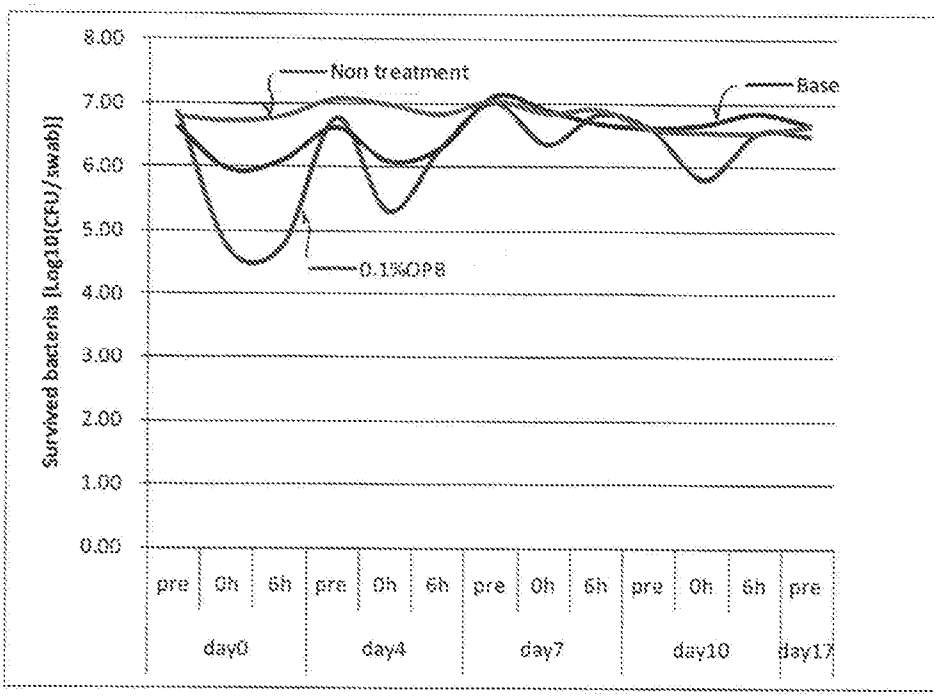
Organ:	Group	Control																							
Histopathological manifestation	Animal No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
	Sample No.	1R	2R	3R	4R	5R	6R	7R	8R	9R	10R	11R	12R	13R	14R	15R	16R	17R	18R	19R	20R	21R	22R	23R	24R
Right cheek pouch, oral mucosa		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Epithelium (cell degeneration, metaplasia, or erosion)		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Leukocyte infiltration		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Vascular congestion		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Edema		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Inflammation index		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Average grade														0											
Other manifestations																									
Intercellular edema		−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
Increased keratosis		−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−
Intraepidermal microabscess		−	−	±	−	−	±	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−	−

Grade in other manifestations: −: within normal limited, ±: very slight, +: slight, 2+: moderate, 3+:severe

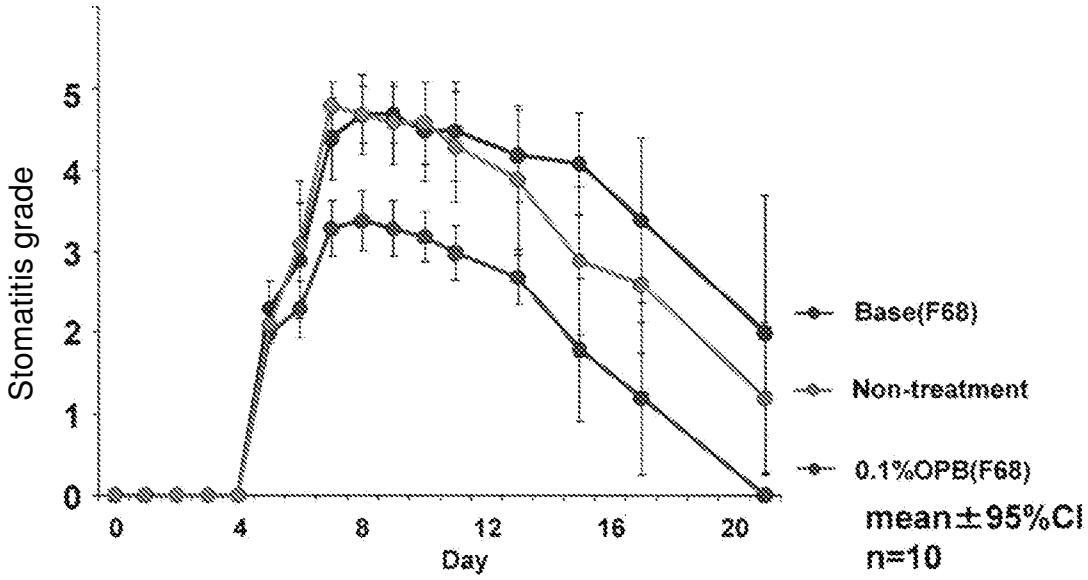
Organ:	Group	Control											
Histopathological manifestation	Animal No.	31	32	33	34	35	36	37	38	39	40	41	42
	Sample No.	31R	32R	33R	34R	35R	36R	37R	38R	39R	40R	41R	42R
Right cheek pouch, oral mucosa		0	0	0	0	0	0	0	0	0	0	0	0
Epithelium (cell degeneration, metaplasia, or erosion)		0	0	0	0	0	0	0	0	0	0	0	0
Leukocyte infiltration		0	0	0	0	0	0	0	0	0	0	0	0
Vascular congestion		0	0	0	0	0	0	0	0	0	0	0	0
Edema		0	0	0	0	0	0	0	0	0	0	0	0
Inflammation index		0	0	0	0	0	0	0	0	0	0	0	0
Average grade								0					
Other manifestations													
Intercellular edema		−	−	−	−	−	−	−	−	−	−	−	−
Increased keratosis		−	−	−	−	−	−	−	−	−	−	−	−
Intraepidermal microabscess		−	−	−	−	−	−	−	−	−	−	±	−

Grade in other manifestations: −: within normal limited, ±: very slight, +: slight, 2+: moderate, 3+:severe

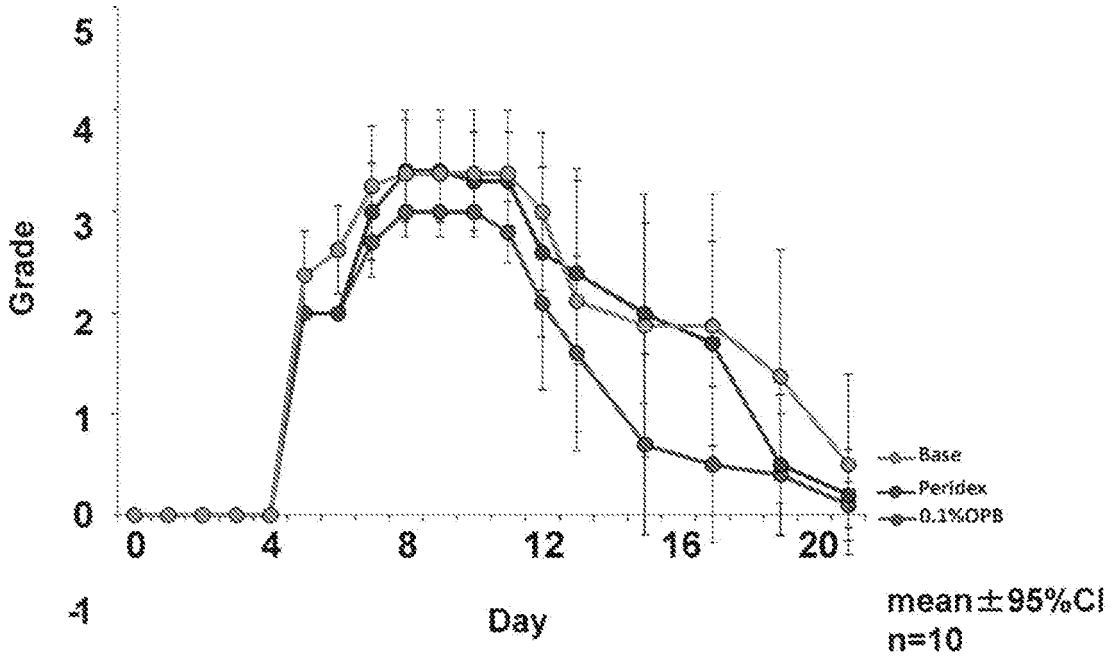
[Fig. 13]


8.00
7.00
6.00
5.00
4.00
3.00
2.00
1.00
0.00
Survived bacteria [Log10(CFU/swab)]
Non treatment
Base
0.1%OPB
pre
0h
6h
day0
day4
day7
day10
day17

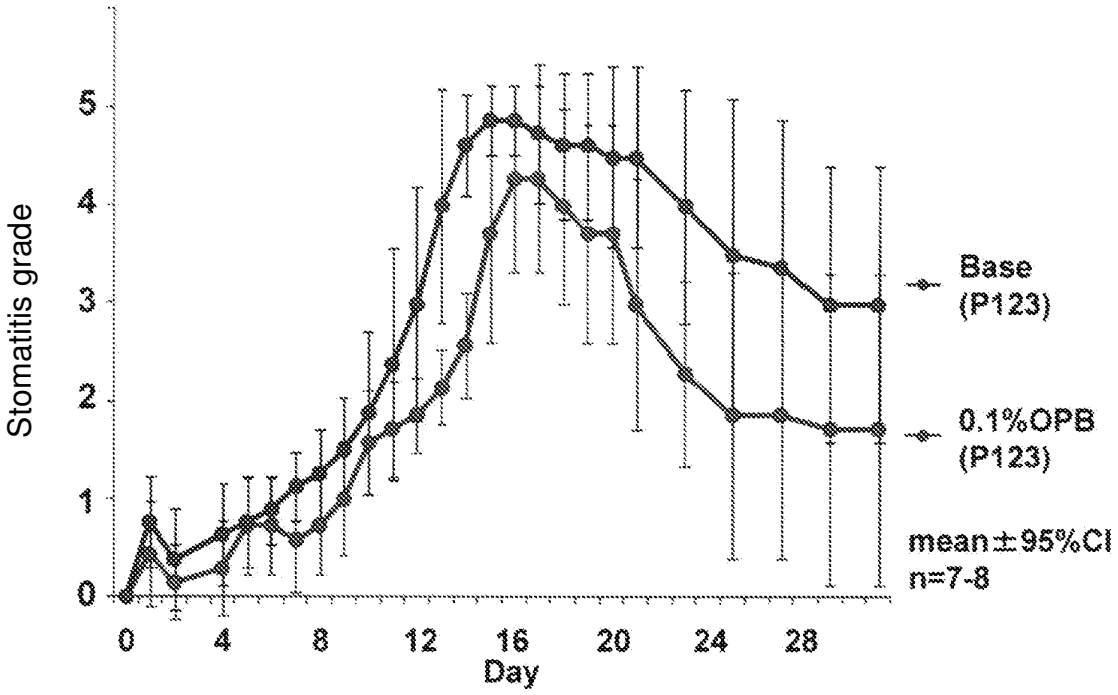
[Fig. 14]


Stomatitis grade
0
1
2
3
4
5
0
4
8
12
16
20
Day
Base(F68)
Non-treatment
0.1%OPB(F68)
mean±95%CI
n=10

[Fig. 15]


Grade
5
4
3
2
1
0
-1
0
4
8
12
16
20
Day
Base
Peridex
0.1%OPB
mean±95%CI
n=10

[Fig. 16]

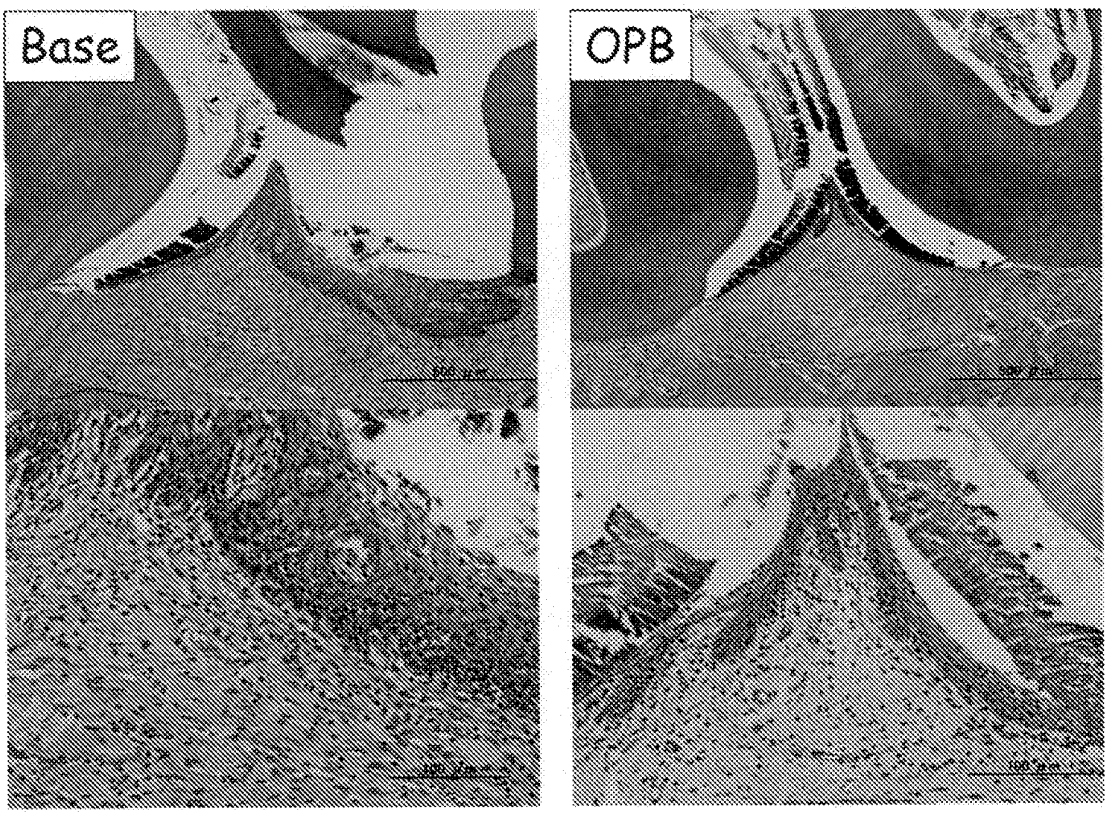

Stomatitis grade
5
4
3
2
1
0
0
4
8
12
16
20
24
28
Day
Base
(P123)
0.1%OPB
(P123)
mean±95%CI
n=7-8

[Fig. 17]

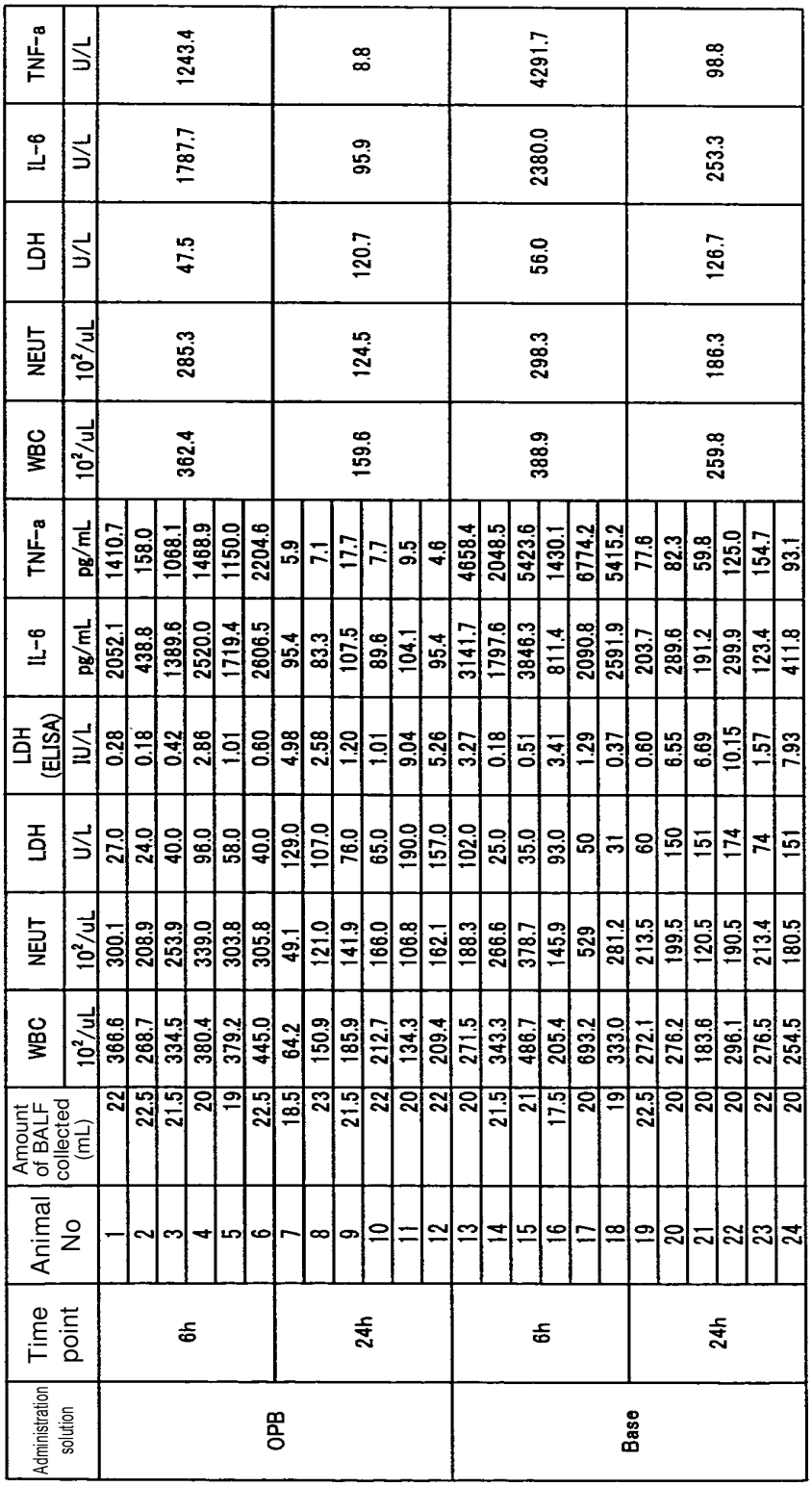
Organ:	Group	OPB										Base									
Histopathological manifestation	Animal No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Stratified squamous epithelium, gingiva																					
Neutrophil infiltration		-	±	±	-	±	±	±	±	±	±	±	±	±	+	±	±	±	±	±	+
Intercellular edematization		-	-	-	-	-	±	-	-	-	-	-	-	-	±	±	-	-	-	-	-
Hyperkeratosis		-	-	-	-	-	-	-	-	-	-	-	-	-	-	±	-	±	-	-	-
Acanthosis		-	-	-	-	-	-	-	-	-	-	-	-	-	±	-	-	±	-	-	-
Erosion		-	-	±	-	-	-	-	-	-	-	-	-	-	-	-	±	-	-	-	-
Basal lamina, gingiva																					
Neutrophil infiltration		±	±	±	±	±	±	±	±	-	-	±	±	-	+	±	+	±	±	±	+
Bleeding		-	-	±	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	±
Edematization		-	-	-	-	-	-	-	-	-	-	-	-	-	±	-	-	-	-	-	-

Grade; - : negative, ±: very slight, +: slight, 2+: moderate, 3+:severe

[Fig. 18]

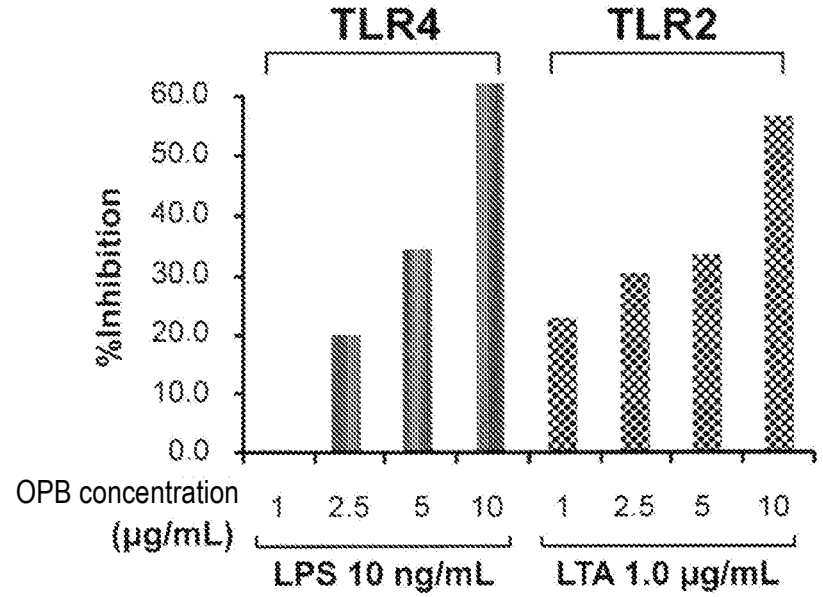


[Fig. 19]

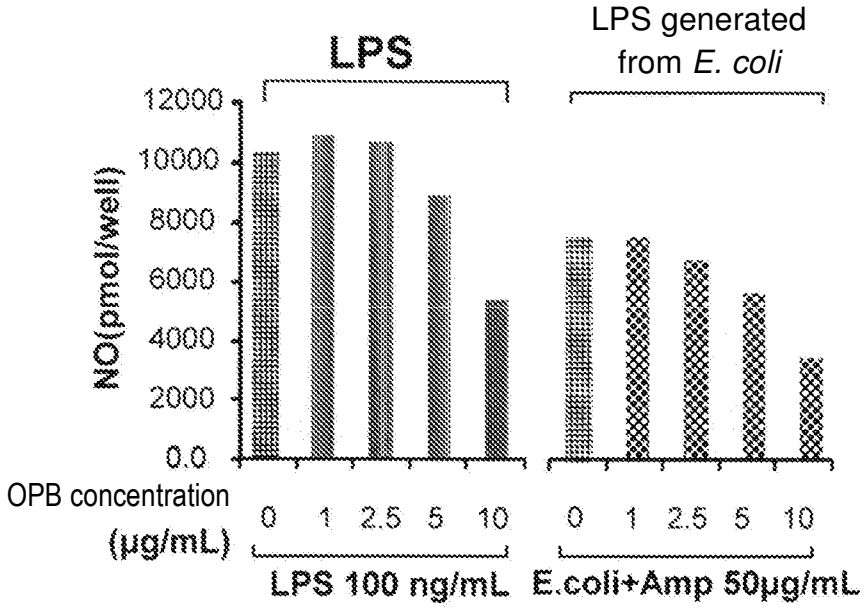


Administration solution	Time point	Animal No	Amount of BALF collected (mL)	WBC	NEUT	LDH	LDH (ELISA)	IL-6	TNF-a	WBC	NEUT	LDH	IL-6	TNF-a
				10^2/uL	10^2/uL	U/L	IU/L	pg/mL	pg/mL	10^2/uL	10^2/uL	U/L	U/L	U/L
OPB	6h	1	22	366.6	300.1	27.0	0.28	2052.1	1410.7	362.4	285.3	47.5	1787.7	1243.4
		2	22.5	268.7	208.9	24.0	0.18	438.8	158.0					
		3	21.5	334.5	253.9	40.0	0.42	1389.6	1068.1					
		4	20	380.4	339.0	96.0	2.86	2520.0	1468.9					
		5	19	379.2	303.8	58.0	1.01	1719.4	1150.0					
		6	22.5	445.0	305.8	40.0	0.60	2606.5	2204.6					
	24h	7	18.5	64.2	49.1	129.0	4.98	95.4	5.9	159.6	124.5	120.7	95.9	8.8
		8	23	150.9	121.0	107.0	2.58	83.3	7.1					
		9	21.5	185.9	141.9	76.0	1.20	107.5	17.7					
		10	22	212.7	166.0	65.0	1.01	89.6	7.7					
		11	20	134.3	106.8	190.0	9.04	104.1	9.5					
		12	22	209.4	162.1	157.0	5.26	95.4	4.6					
Base	6h	13	20	271.5	188.3	102.0	3.27	3141.7	4658.4	388.9	298.3	56.0	2380.0	4291.7
		14	21.5	343.3	266.6	25.0	0.18	1797.6	2048.5					
		15	21	486.7	378.7	35.0	0.51	3846.3	5423.6					
		16	17.5	205.4	145.9	93.0	3.41	811.4	1430.1					
		17	20	693.2	529	50	1.29	2090.8	6774.2					
		18	19	333.0	281.2	31	0.37	2591.9	5415.2					
	24h	19	22.5	272.1	213.5	60	0.60	203.7	77.6	259.8	186.3	126.7	253.3	98.8
		20	20	276.2	199.5	150	6.55	289.6	82.3					
		21	20	183.6	120.5	151	6.69	191.2	59.8					
		22	20	296.1	190.5	174	10.15	299.9	125.0					
		23	22	276.5	213.4	74	1.57	123.4	154.7					
		24	20	254.5	180.5	151	7.93	411.8	93.1					

[Fig. 20]


TLR4
TLR2
60.0
50.0
40.0
30.0
20.0
10.0
0.0
%Inhibition
OPB concentration
(μg/mL)
1
2.5
5
10
1
2.5
5
10
LPS 10 ng/mL
LTA 1.0 μg/mL

[Fig. 21]


LPS
LPS generated
from E. coli
12000
10000
8000
6000
4000
2000
0.0
NO(pmol/well)
OPB concentration
(μg/mL)
0
1
2.5
5
10
0
1
2.5
5
10
LPS 100 ng/mL
E.coli+Amp 50μg/mL