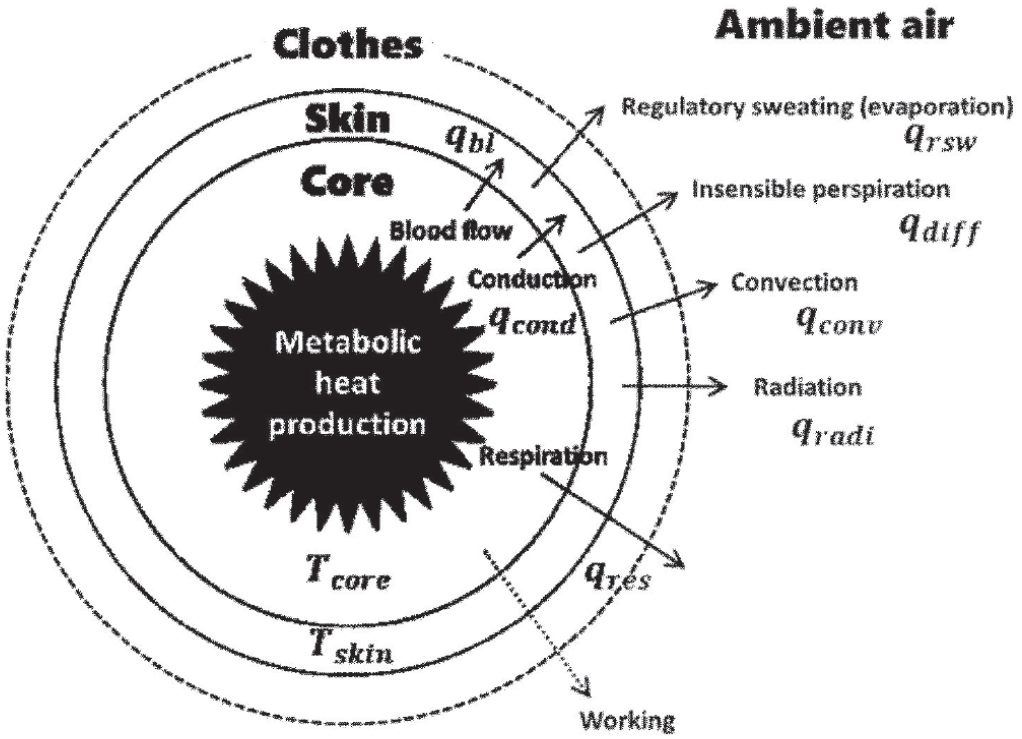
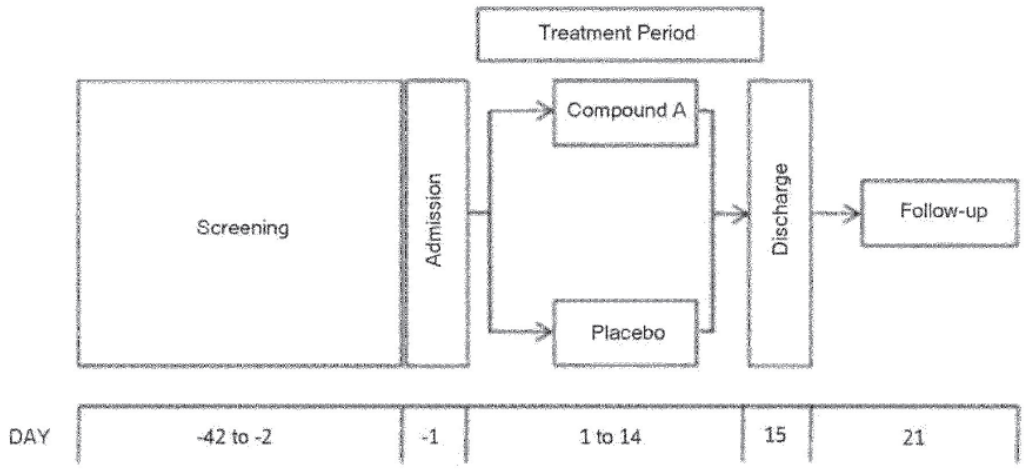
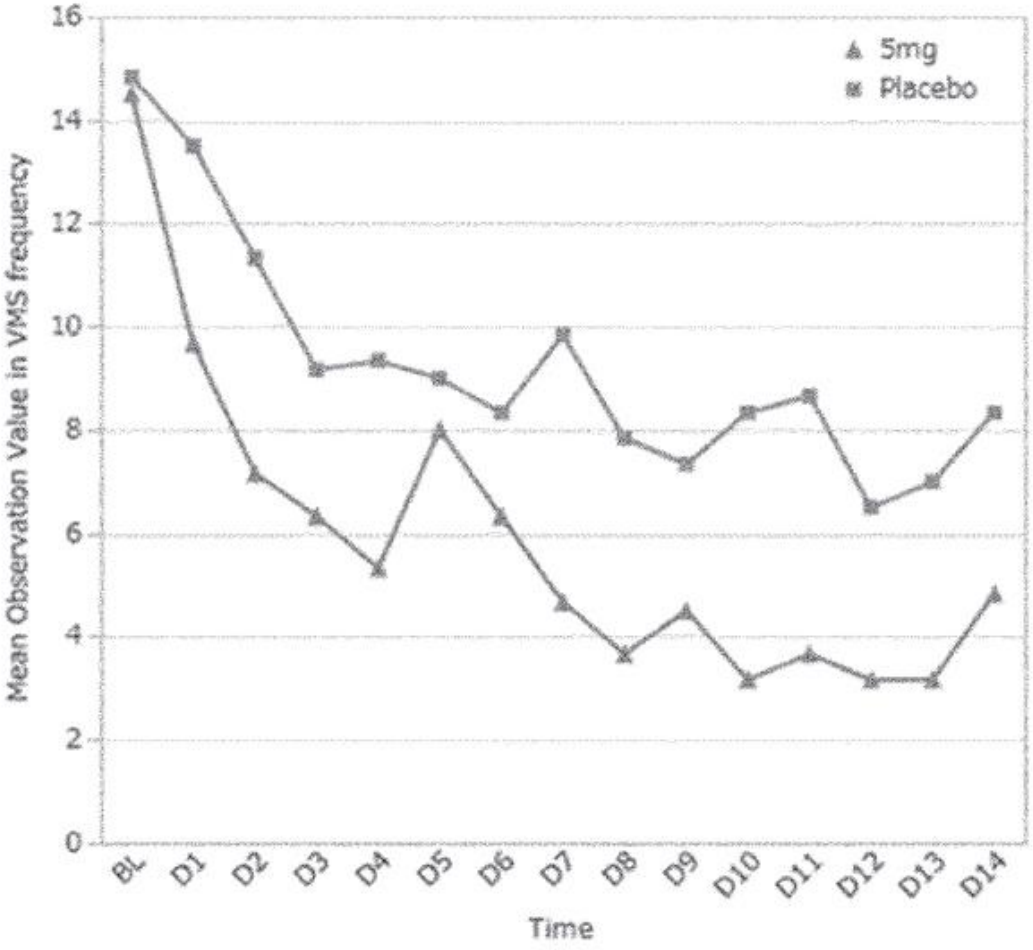
[Fig. 1]


Clothes
Ambient air
Skin
Core
q_{bl}
Blood flow
Conduction
q_{cond}
Metabolic heat production
T_{core}
T_{skin}
Regulatory sweating (evaporation)
q_{rsw}
Insensible perspiration
q_{diff}
Convection
q_{conv}
Radiation
q_{radi}
Respiration
q_{res}
Working

[Fig. 2]


Treatment Period
Screening
Admission
Compound A
Placebo
Discharge
Follow-up
DAY
-42 to -2
-1
1 to 14
15
21

[Fig. 3]


5mg
Placebo
Mean Observation Value in VMS frequency
0
2
4
6
8
10
12
14
16
BL
D1
D2
D3
D4
D5
D6
D7
D8
D9
D10
D11
D12
D13
D14
Time

[Fig. 4]

Fig. 4A

Placebo group

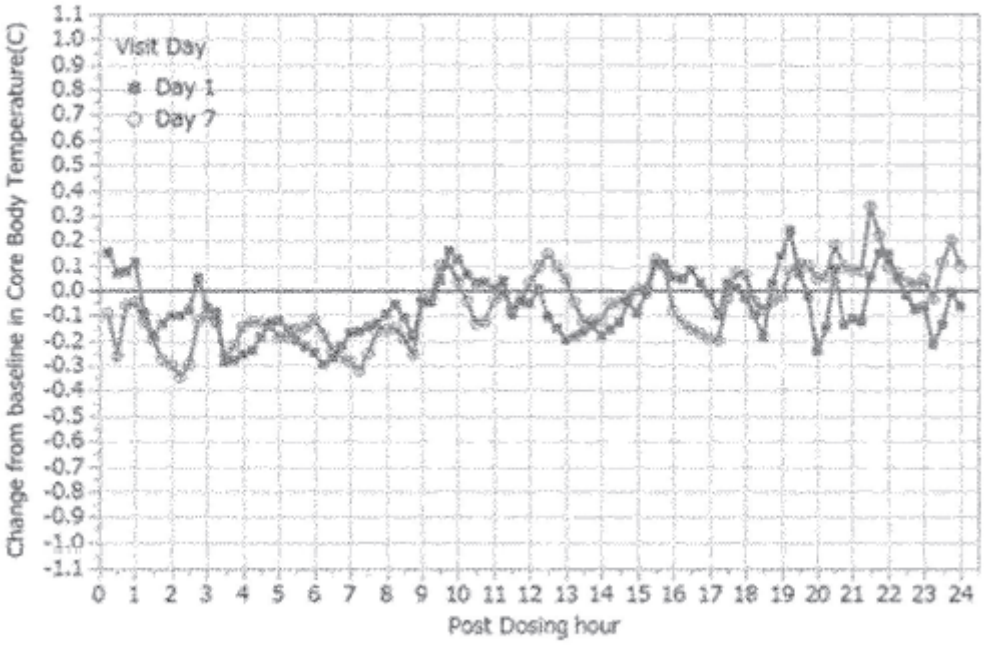
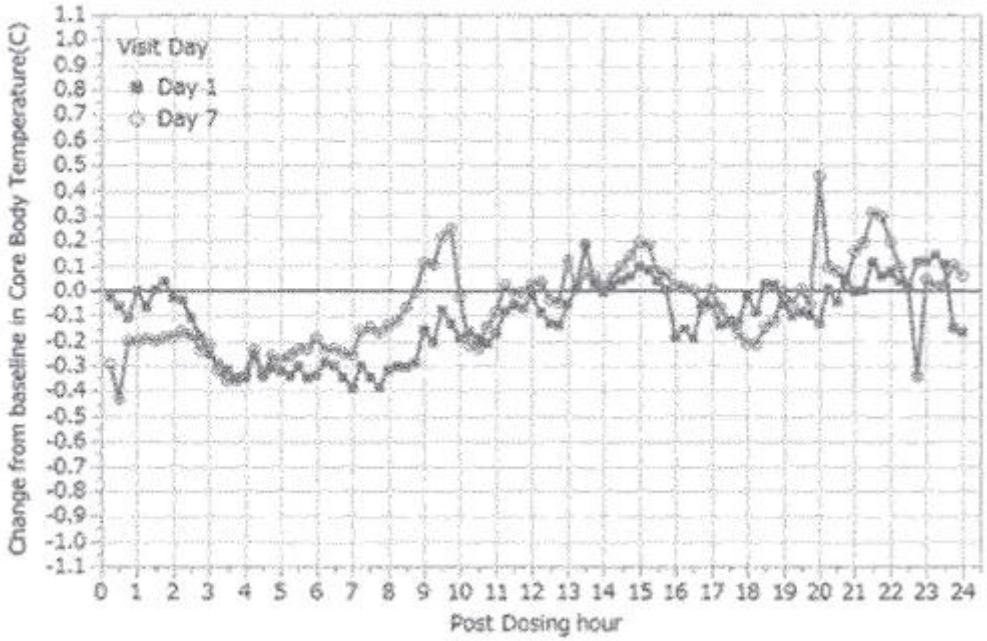


Fig. 4B

5mg administered group



[Fig. 5]

Fig. 5A

20mg administered group

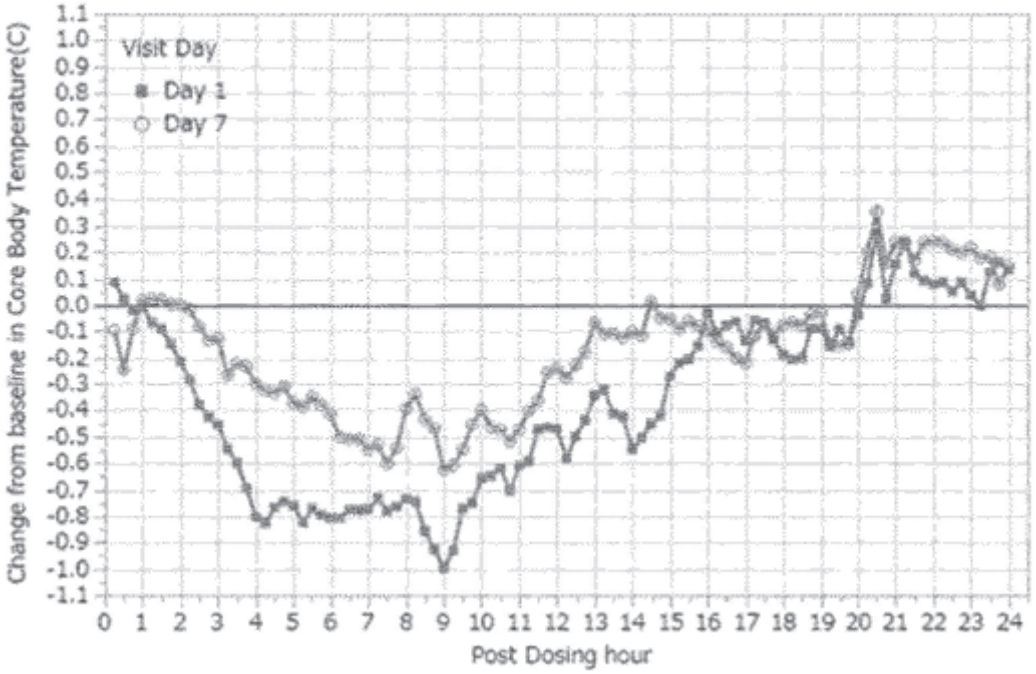
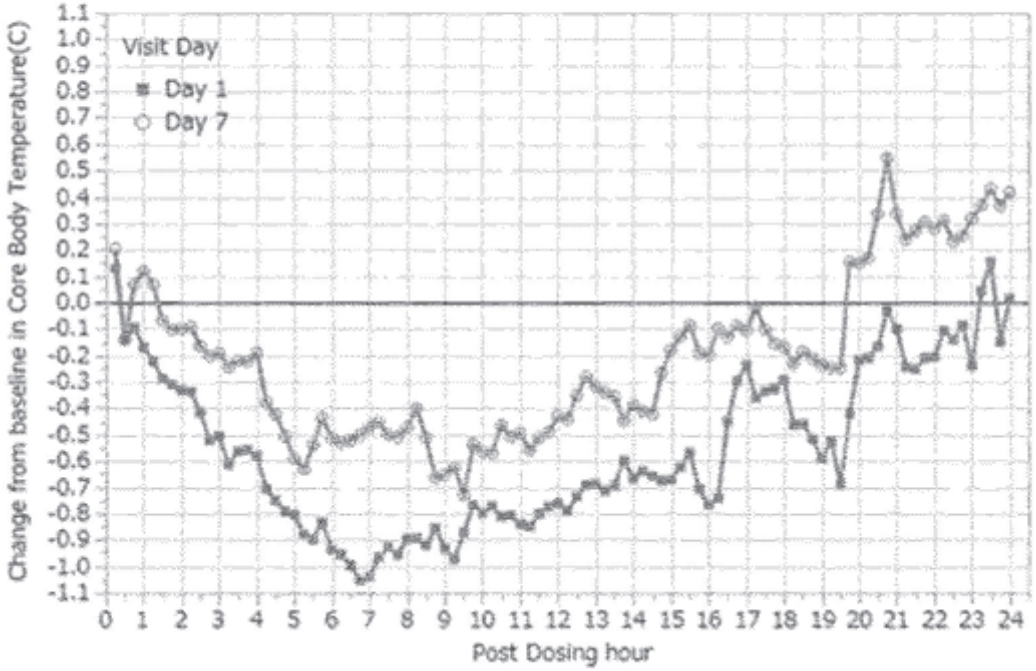
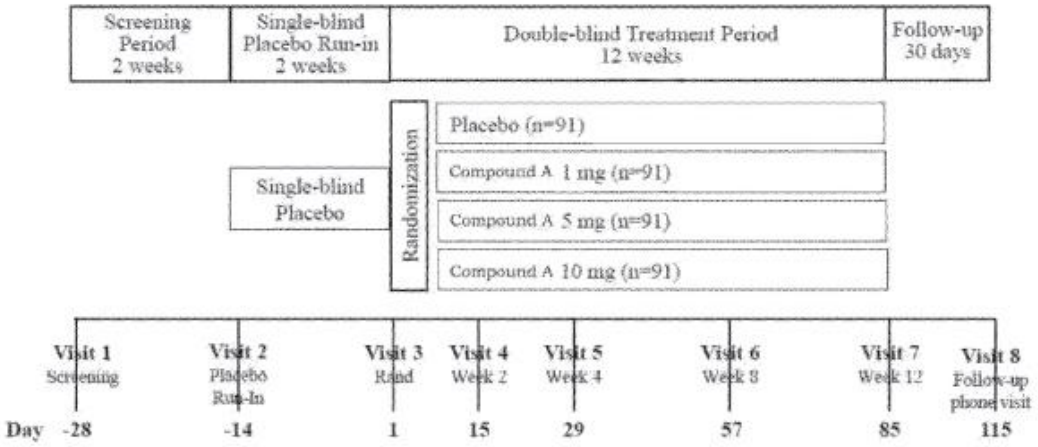


Fig. 5B

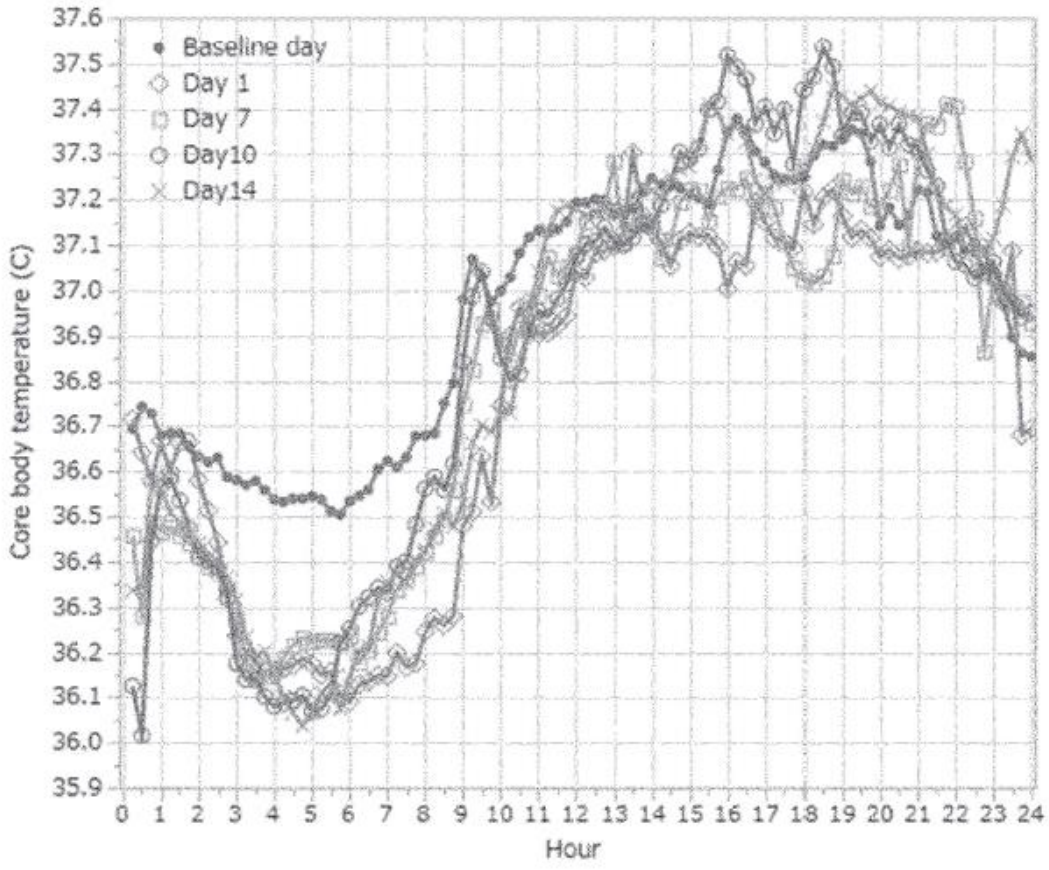
50mg administered group



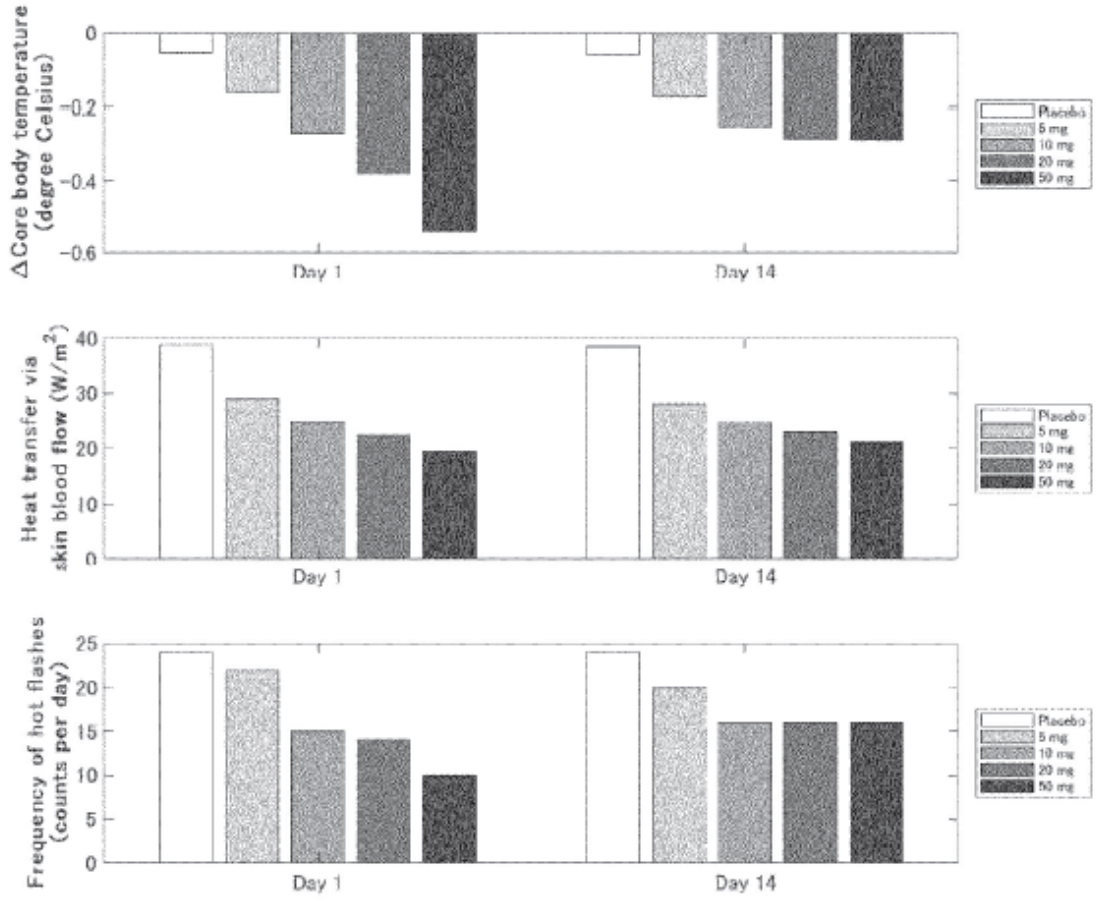
[Fig. 6]


Screening Period 2 weeks
Single-blind Placebo Run-in 2 weeks
Double-blind Treatment Period 12 weeks
Follow-up 30 days
Single-blind Placebo
Randomization
Placebo (n=91)
Compound A 1 mg (n=91)
Compound A 5 mg (n=91)
Compound A 10 mg (n=91)
Visit 1 Screening
Visit 2 Placebo Run-In
Visit 3 Rand
Visit 4 Week 2
Visit 5 Week 4
Visit 6 Week 8
Visit 7 Week 12
Visit 8 Follow-up phone visit
Day -28
-14
1
15
29
57
85
115

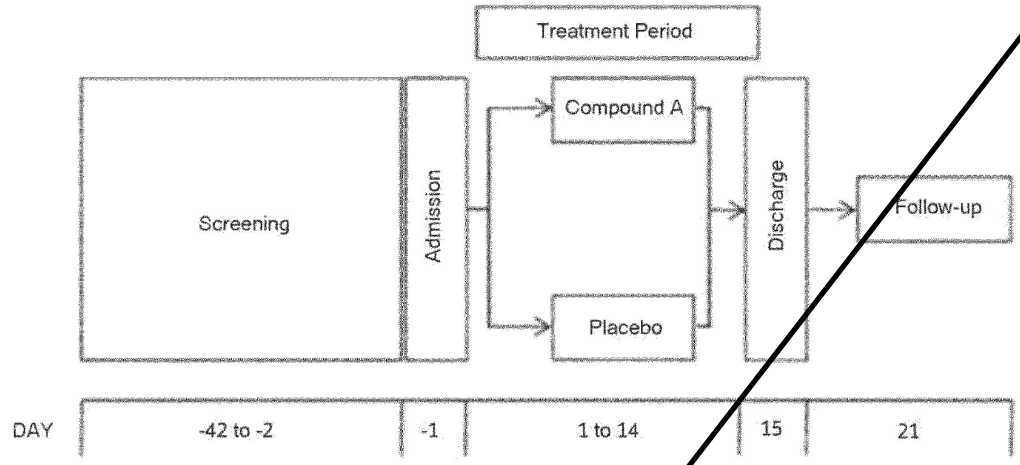
[Fig. 7]


Baseline day
Day 1
Day 7
Day10
Day14
Core body temperature (C)
37.6
37.5
37.4
37.3
37.2
37.1
37.0
36.9
36.8
36.7
36.6
36.5
36.4
36.3
36.2
36.1
36.0
35.9
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24
Hour

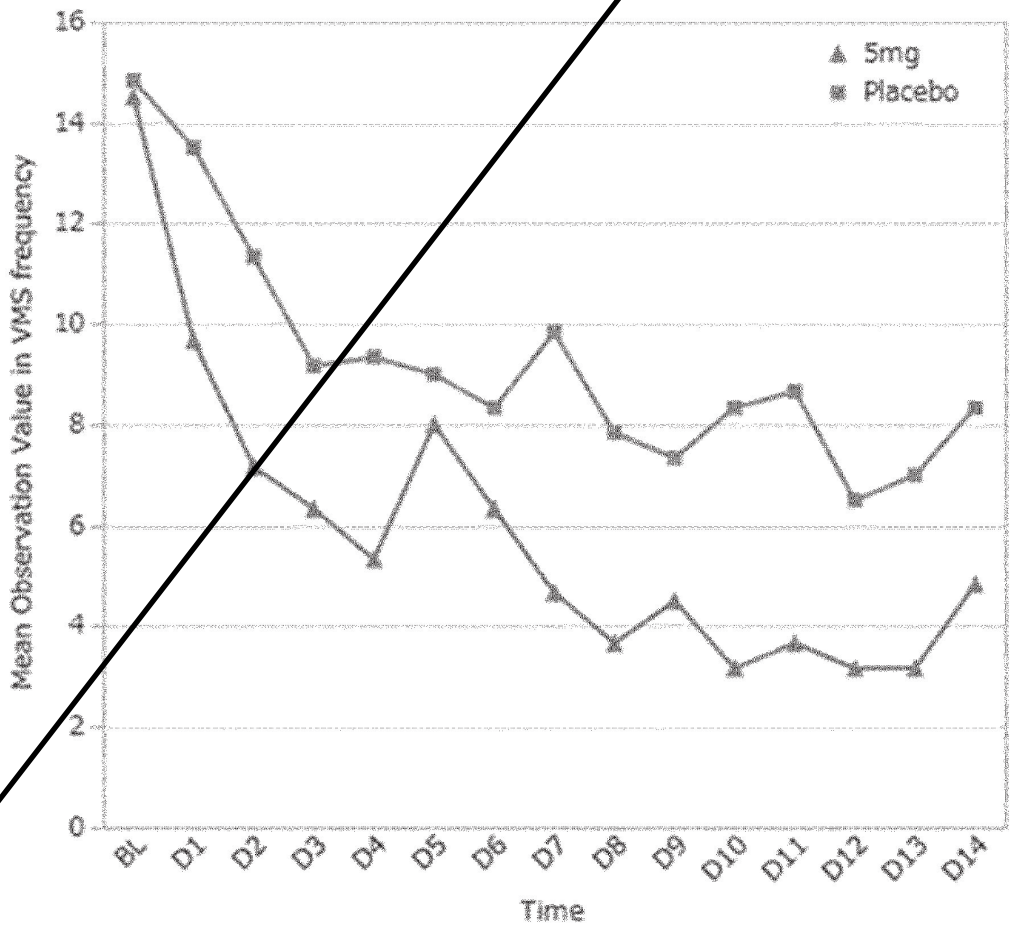
[Fig. 8]


ΔCore body temperature (degree Celsius)
0
−0.2
−0.4
−0.6
Day 1
Day 14
Placebo
5 mg
10 mg
20 mg
50 mg
Heat transfer via skin blood flow (W/m²)
40
30
20
10
0
Day 1
Day 14
Placebo
5 mg
10 mg
20 mg
50 mg
Frequency of hot flashes (counts per day)
25
20
15
10
5
0
Day 1
Day 14
Placebo
5 mg
10 mg
20 mg
50 mg

[Fig. 1]


Treatment Period
Screening
Admission
Compound A
Placebo
Discharge
Follow-up
DAY
-42 to -2
-1
1 to 14
15
21

[Fig. 2]


5mg
Placebo
Mean Observation Value in VMS frequency
0
2
4
6
8
10
12
14
16
BL
D1
D2
D3
D4
D5
D6
D7
D8
D9
D10
D11
D12
D13
D14
Time

[Fig. 3]

Fig. 3A

Placebo group

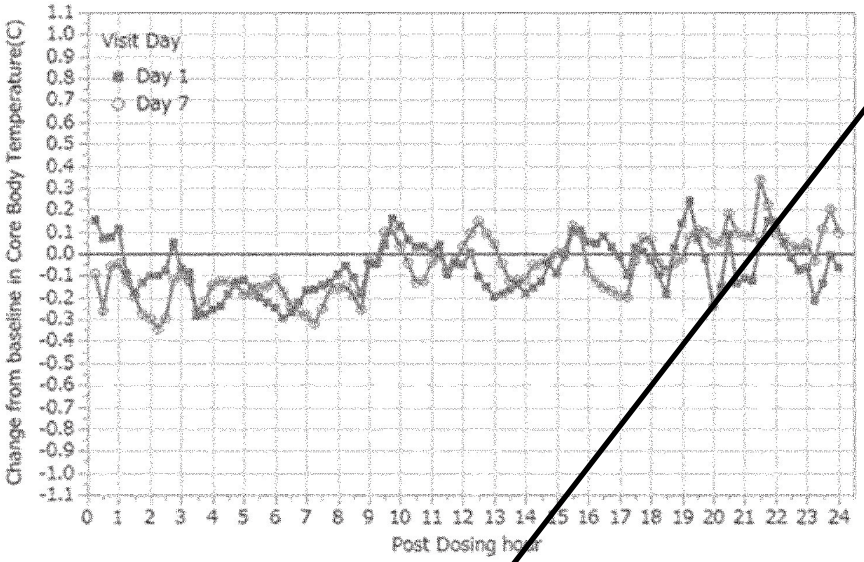
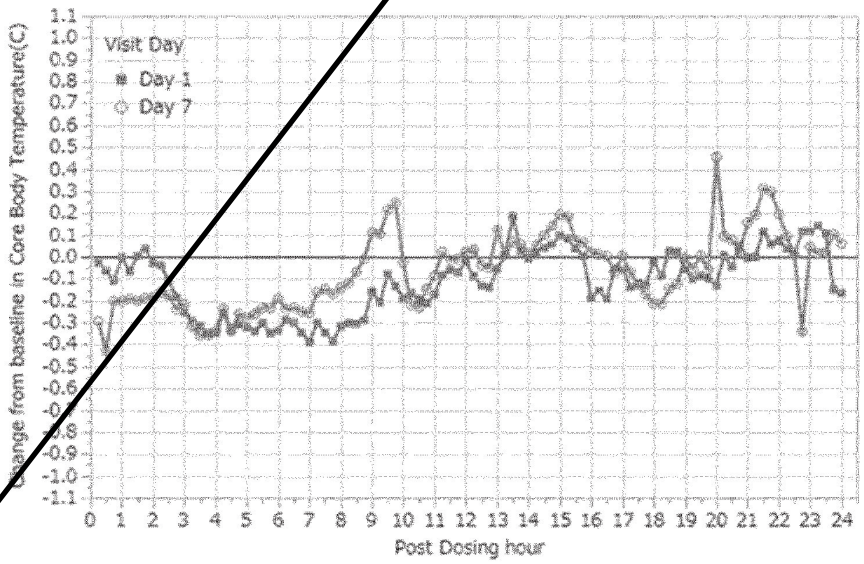


Fig. 3B

5mg administered group



[Fig. 4]

Fig. 4A

20mg administered group

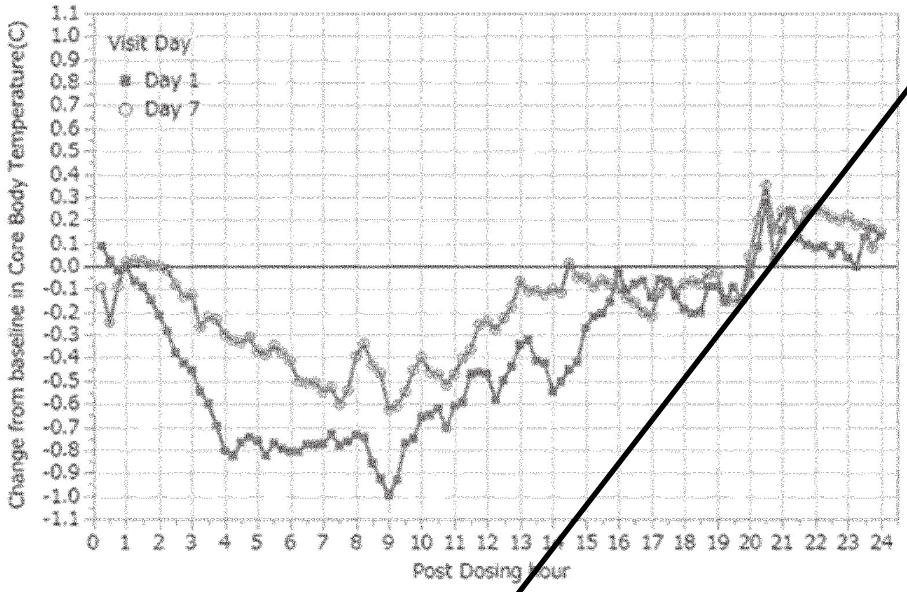
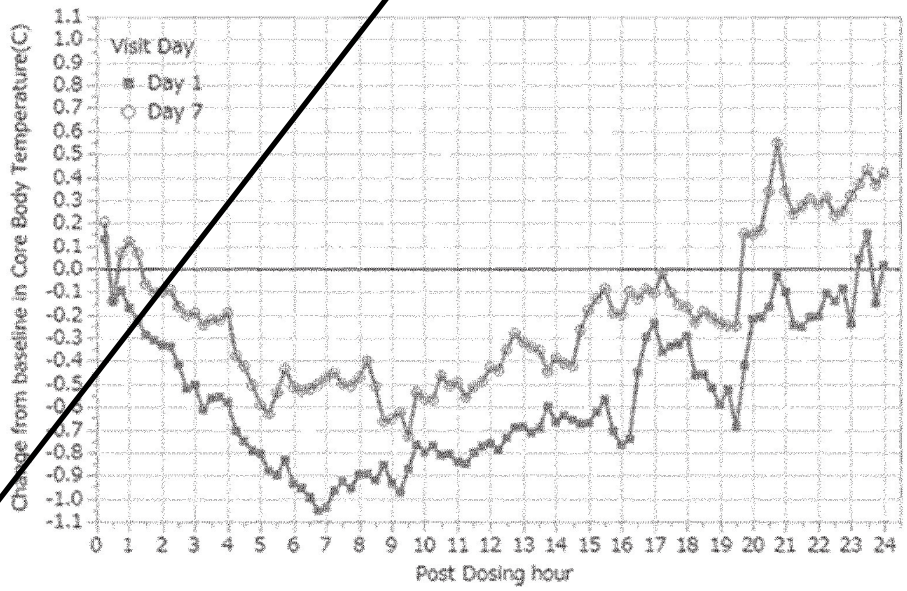
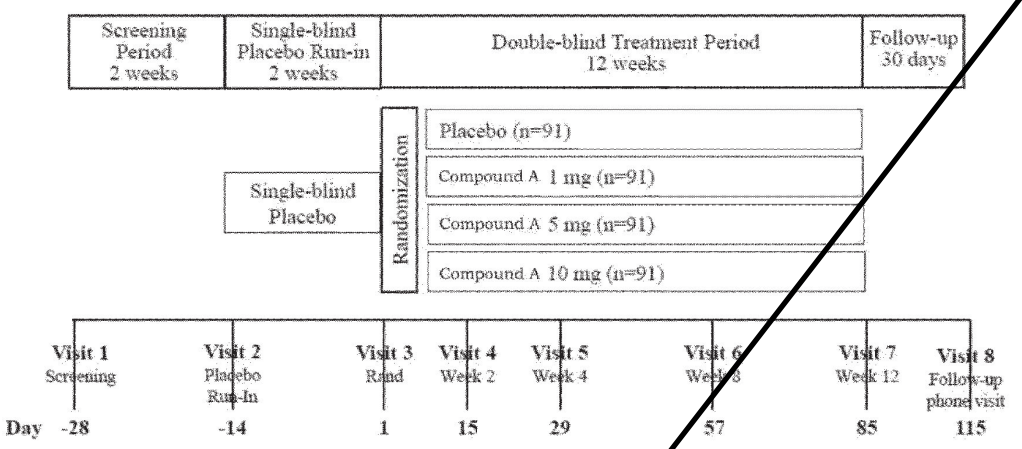


Fig. 4B

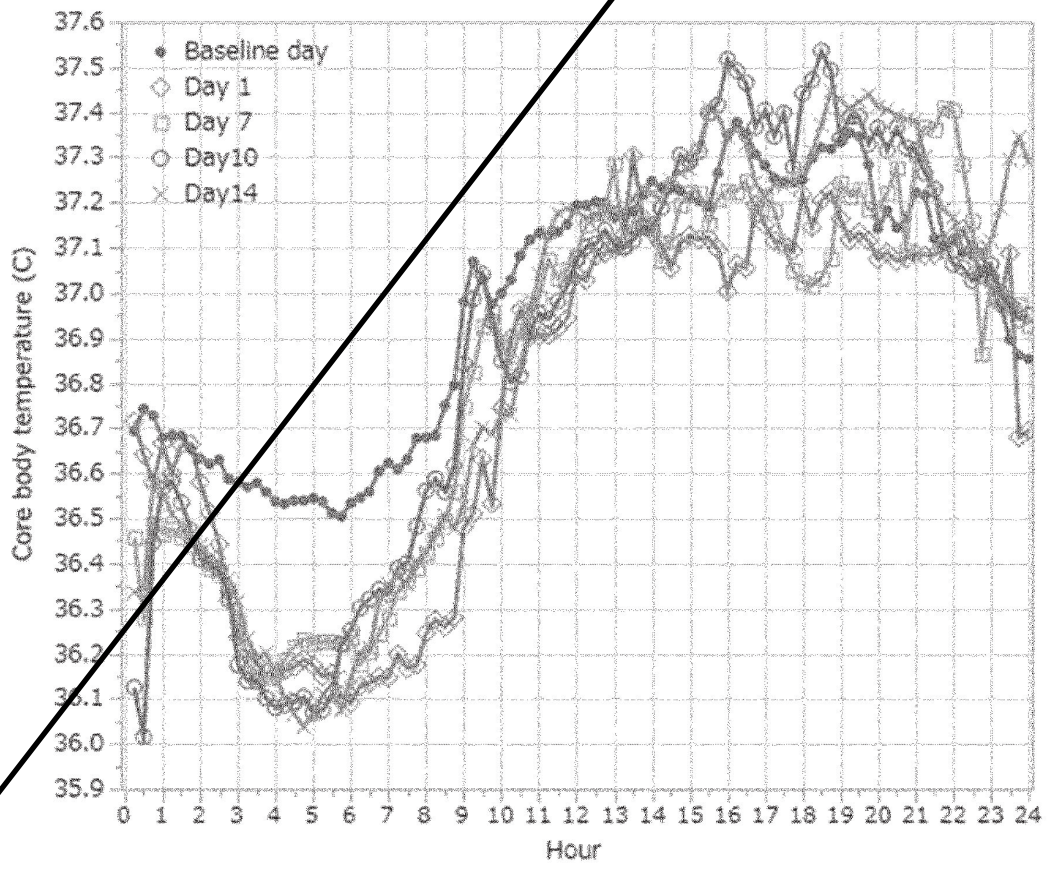
50mg administered group



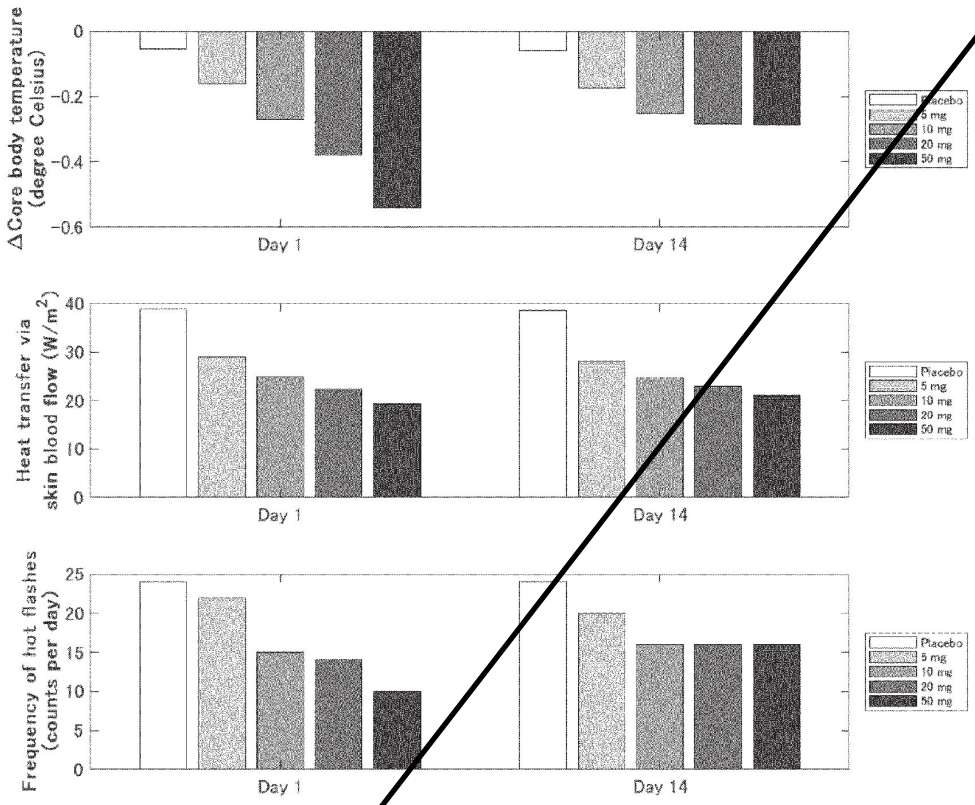
[Fig. 5]


Screening Period 2 weeks
Single-blind Placebo Run-in 2 weeks
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Single-blind Placebo
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Placebo (n=91)
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Compound A 10 mg (n=91)
Visit 1 Screening
Visit 2 Placebo Run-In
Visit 3 Rand
Visit 4 Week 2
Visit 5 Week 4
Visit 6 Week 8
Visit 7 Week 12
Visit 8 Follow-up phone visit
Day -28
-14
1
15
29
57
85
115

[Fig. 6]


Baseline day
Day 1
Day 7
Day10
Day14
Core body temperature (C)
Hour
37.6
37.5
37.4
37.3
37.2
37.1
37.0
36.9
36.8
36.7
36.6
36.5
36.4
36.3
36.2
36.1
36.0
35.9
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24

[Fig. 7]


ΔCore body temperature (degree Celsius)
0
-0.2
-0.4
-0.6
Day 1
Day 14
Placebo
5 mg
10 mg
20 mg
50 mg
Heat transfer via skin blood flow (W/m2)
40
30
20
10
0
Day 1
Day 14
Placebo
5 mg
10 mg
20 mg
50 mg
Frequency of hot flashes (counts per day)
25
20
15
10
5
0
Day 1
Day 14
Placebo
5 mg
10 mg
20 mg
50 mg