



MIF-1

E

Tyr-

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:

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,

, 2013 .



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-

MIF-1

-

E

Tyr-

:

“ ”

: 03.01.05.

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,

:

1.

.

,

2.

. -

,

, 2013 .

1 . 132 294 , 33 1
293 . ,

, - 10.12.2013 .

” 2 , 07.06.2013 . 15.00
” 2, 36-196/ 05.02.2013 .

1. . - , - , -
() ;

:

2. . - , - , -
() ;

3. . - , - - () ;

4. . - , - - () ;

5. . - , - - ()

:

1. . - , - , -

2. . - , . - -

” 2. , , -

NH₃

L-canavanine

MIF-1

Tyr-MIF-1.

NO-

Tyr-MIF-1

1.

; 2.

Tyr-MIF-1

Tyr-MIF-1,

; 5.

Tyr-MIF-1

; 6.

nNOS u NADPH-d

PAG.

e :
 Tyr-MIF-1; Tyr-Orn-MIF-1, Tyr-Cit-MIF-1, Tyr-Cav-
 MIF-1, Tyr-Can-MIF-1; -
 - Tyr-Cit-MIF-1, Tyr-Cav-MIF-1 ,
 - ; ,
 ; Tyr-Cit-MIF-1, Tyr-Cav-MIF-1
 (NOS) periaqueductal grey
 (PAG).

1. :
 ➤ ;
 ➤ Tyr-Orn-MIF-1, Tyr-Cit-MIF-1, Tyr-Cav-MIF-1, Tyr-Can-
 MIF-1 ;

2. , -
 Tyr-Cit-MIF-1 Tyr-Cav-MIF-1 ,
 - ;

3. :
 ➤ Tyr-Cit-MIF-1 Tyr-Cav-MIF-1 ,
 - ;

4. :
 ➤ Tyr-Cit-MIF-1 Tyr-Cav-MIF-1 ,
 - ;

5. Tyr-Cit-MIF-1, Tyr-Cav-MIF-1 :
 ➤ (NOS) periaqueductal grey (PAG).

424 Wistar
 (180-200g). - 22
 $\pm 2^\circ$, : 12
 /12 . 9.00 12.00 .

(Zimmermann M., 1983) - .

I. *In vivo*

1.

1.1.

- *aw pressure (PP) test*

e Ugo Basille.

“ ”

(500).

(Randall-Selitto, 1957).

1.2.

- *Hot plate (HP) test*

(55 \pm 1)

(),

. Cut off – 30 sec.

2.

2.1.

- 1

(.3).

2.2.

4° C 1 .

2.3.

II. *In vitro*

: (40 mg/kg, i.p.)

4% 0.1 pH 7.2-7.4.
, 1 .
0.1 , 7.4,
4°C.
(Reihart-Jung),
40 μm .

X

NADPH-diaphorase (NADPH-d) NOS (Scherer-Singler et al. 1983).

NOS

NOS-

Olympus CUE2.

Olympus-CUE2.

ANOVA,

<0.05.

(x ± SEM).

_____ :

: 6.

0.9%- NaCl

(i.p.) - , 1 mg/kg

Tyr-Cit-MIF-1, Tyr-Cav-MIF-1: 1.) ; 2.)

; 3.) 20 . Naloxone hydrochloride dehydrate (Nal, 1 mg/kg), L-N^G-Nitro-Arginine Methyl Ester (L-NAME, 10 mg/kg) L-Arginine (L-Arg, 1 mg/kg), ethylene blue (MB, 500µg/rat), SIN-1, 0,2 mg/kg, i.p).

1 ml/kg.

15 .

: (40 mg/kg, i.p.)

4%

0.1

pH 7.2-7.4.

, 1 .

0.1

, 7.4,

4°C.

(Reihart-Jung),

40 µm .

1.

Tyr-MIF-1

Tyr-Orn-MIF-1, Tyr-Cit-MIF-1 Tyr-Cav-MIF-1 (1 mg/kg, i.p.)

(p < 0.01)

Tyr-Cit-MIF-1 (p < 0.05) Tyr-Cav-

MIF-1 (p<0.05)

Tyr-MIF-1.

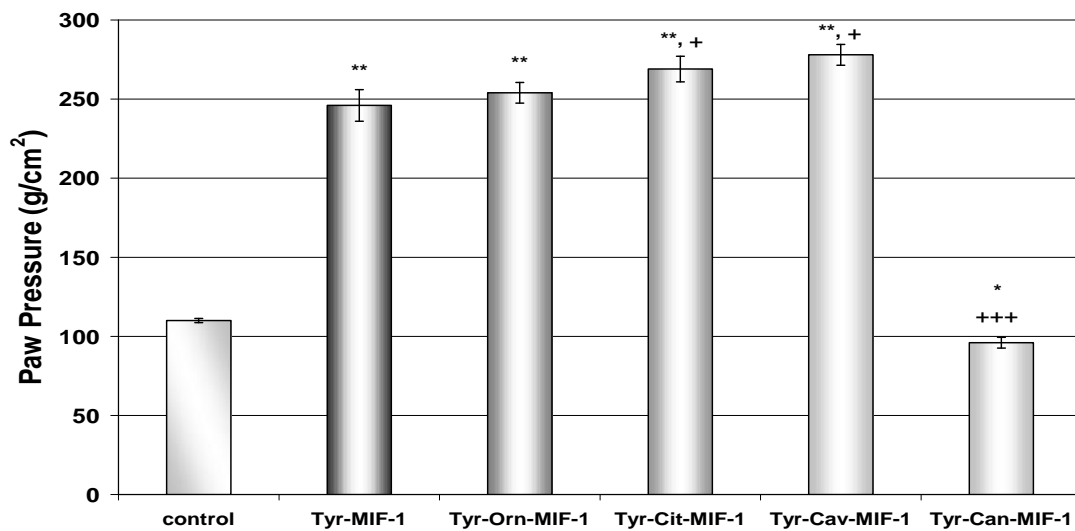
Tyr-Can-MIF-1

(p < 0.05)

Tyr-MIF-1

-

(. 1).



. 1. Tyr-Orn-MIF-1, Tyr-Cit-MIF-1 Tyr-Cav-MIF-1 Tyr-Can-MIF-1 (1 mg/kg, i.p.)

P

È S.E.M.;

*P<0.05, **P<0.01

; +P<0.05, +++P<0.001

Tyr-MIF-1.

-

-

..

Tyr-Orn-MIF-1 (p < 0.01), Tyr-Cit-

MIF-1 (p < 0.01) Tyr-Cav-MIF-1 (p<0.001)

Tyr-Can-MIF-1

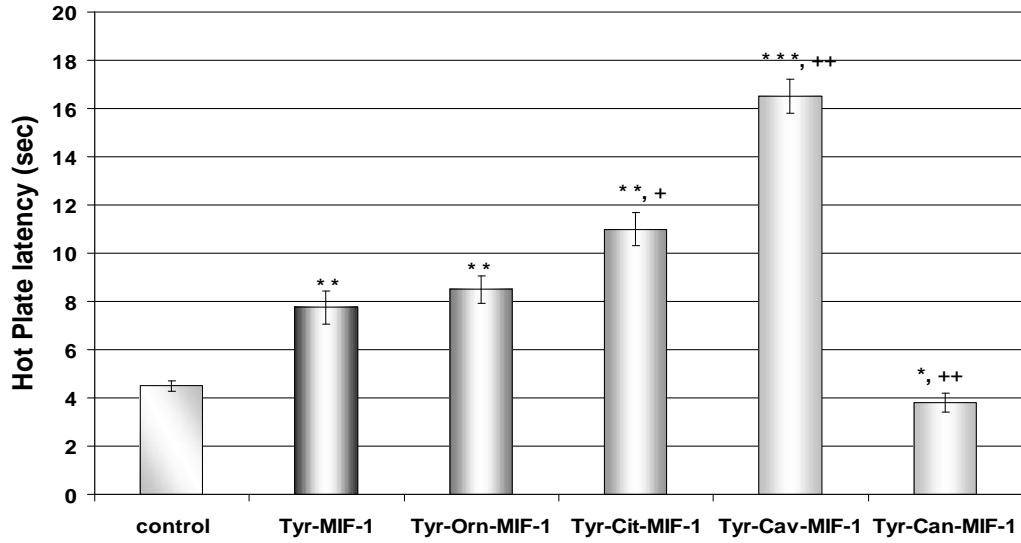
.

Tyr-Cit-MIF-1 (p < 0.05) Tyr-Cav-MIF-1 (p<

0.01)

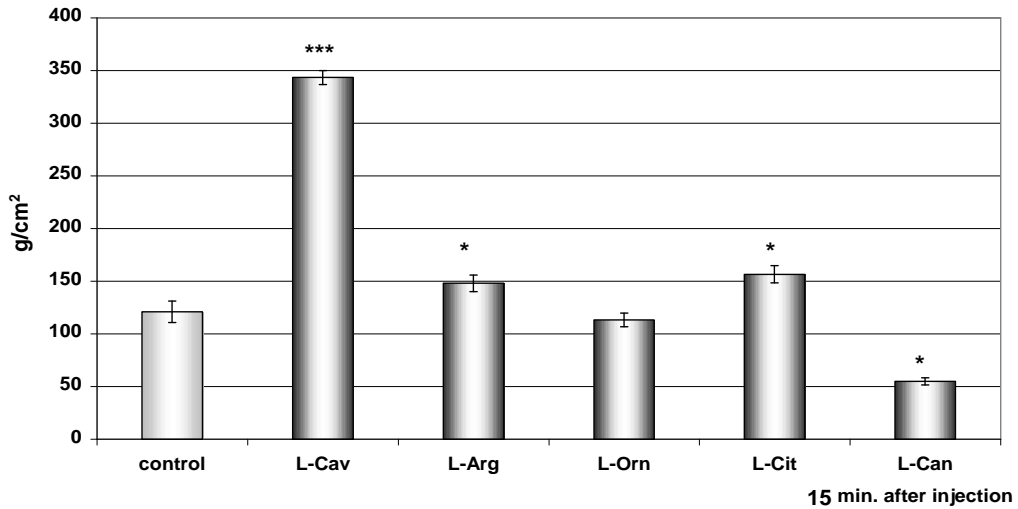
-

Tyr-MIF-1 (. 2).



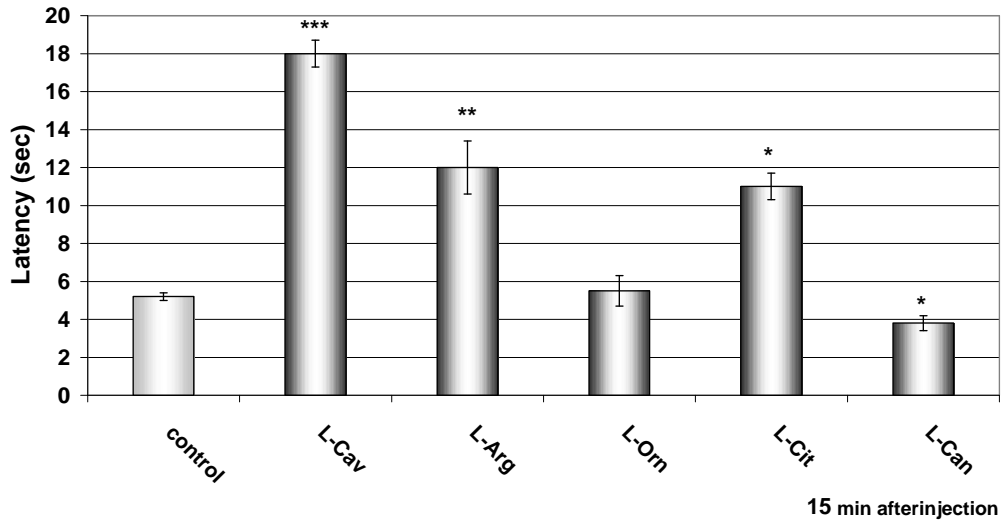
2. Tyr-Orn-MIF-1, Tyr-Cit-MIF-1, Tyr-Cav-MIF-1 Tyr-Can-MIF-1 (1 mg/kg, i.p.)
 - HP
 S.E.M.; * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$; + $P < 0.05$, ++ $P < 0.01$ Tyr-MIF-1.

PAW PRESSURE



3. L-Cav, L-arg, L-Orn, L-Cit L-Can (1 mg/kg, i.p.)
 P S.E.M.; * $P < 0.05$, ** $P < 0.01$
 ; + $P < 0.05$, +++ $P < 0.001$ Tyr-MIF-1.

HOT PLATE



4. L-Cav, L-arg, L-Orn, L-Cit L-Can (1 mg/kg, i.p.) -
 HP . S.E.M.; *P<0.05,
 P<0.01, *P<0.001 ; +P<0.05, ++P<0.01 Tyr-MIF-1.

- L-canavanine, L-
 citruline L-ornitine.

:
 ➤ Tyr-MIF-1
 Tyr-MIF-1
 ➤ Tyr-Cit-MIF-1 Tyr-Cav-MIF-1 -
 L-Cit L-Cav

II.

Tyr-Cit-MIF-1, Tyr-Cav-MIF-1
SIA

, Tyr-Cit-MIF-1

(<0.01) - - - 15 30

(.3 4).

Tyr-Cav-MIF-1 (<0.01)

- , - - 15 30

(.5

.6).

Tyr-Cav-MIF-1 15 - 30

Tyr-Cit-MIF-1 (.3 5

.4 6).

Tyr-MIF-1

(-) - (-)

(.3 5 .4 6).

, 1 (1h IS)

15 (<0.01) 30 (<0.01) (.3).

1h IS

15 . (<0.01) (.4).

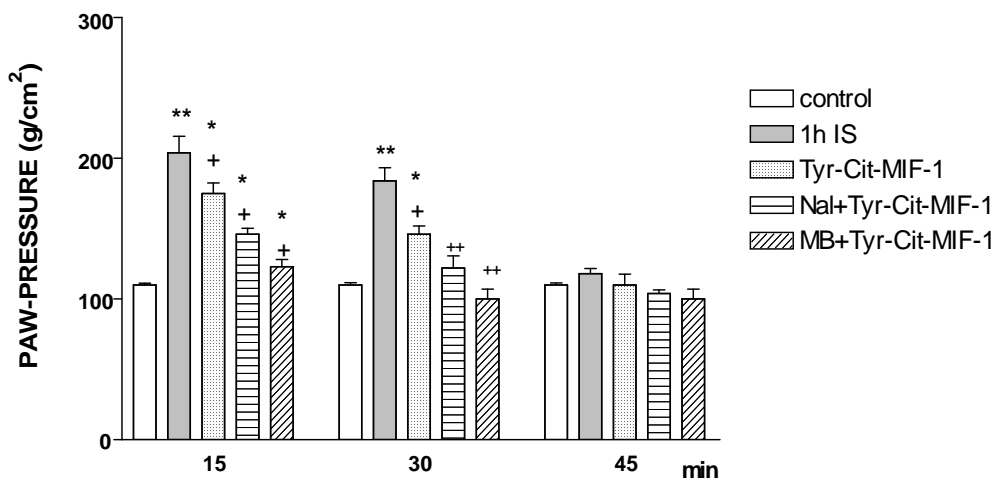
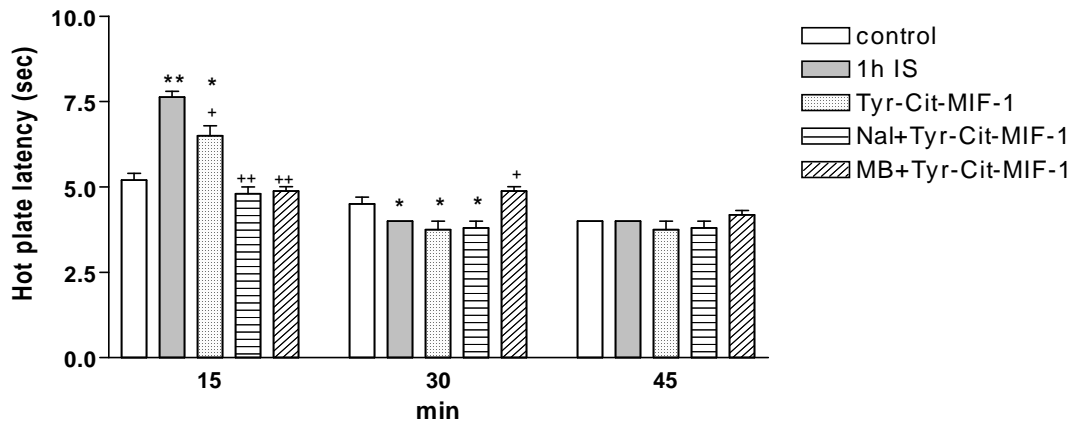
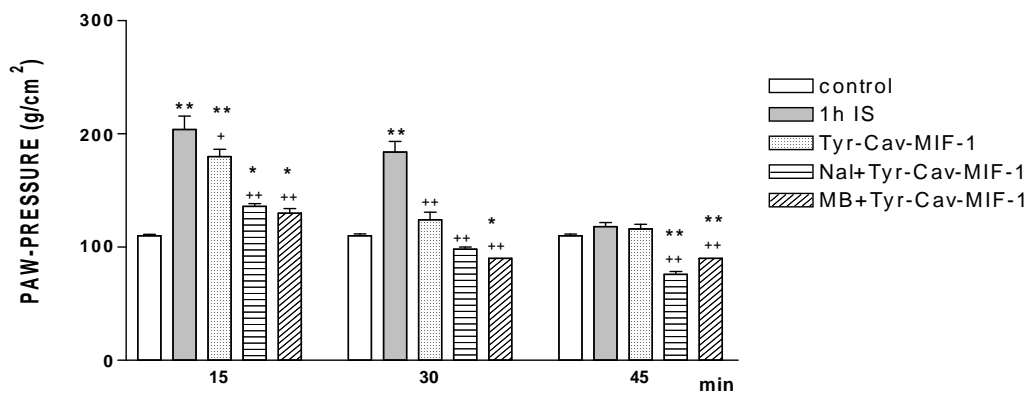


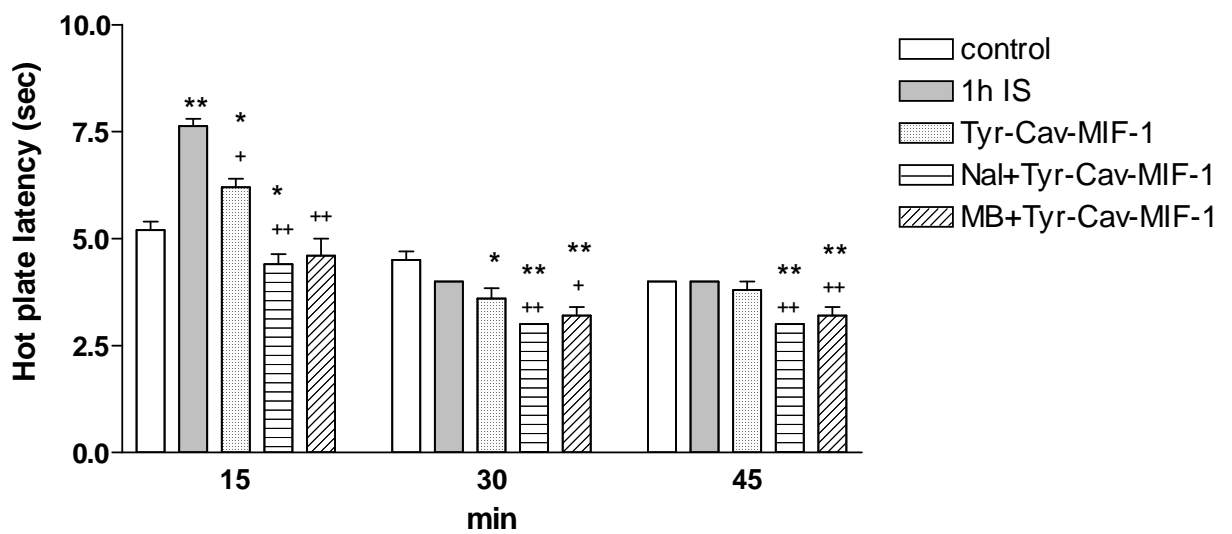
Fig. 5. Tyr-Cit-MIF-1 (500µg/rat) (Nal)(1h IS) P . (Nal)(1h IS) S.E.M.; *P<0.05, **P<0.01; +P<0.05, ++P<0.01 1h IS.



6. Tyr-Cit-MIF-1 (500µg/rat) (Nal) (1 mg/kg, 1h IS) HP
 i.p.) - S.E.M.; *P<0.05, **P<0.01
 ; +P<0.05; ++P<0.01 1h IS.



7. Tyr-Cav-MIF-1 (500µg/rat) (Nal) (1 mg/kg, 1h IS) HP
 mg/kg, i.p.) - S.E.M.; *P<0.05, **P<0.01
 P ; +P<0.05, ++P<0.01 1h IS.



8. Tyr-Cav-MIF-1 (500µg/rat) (Nal) (1 mg/kg, 1h IS) HP
 mg/kg, i.p.) - S.E.M.; *P<0.05, **P<0.01
 IS) HP ; +P<0.05; ++P<0.01 1h IS.

SIA,

(1 mg/kg, i.p.)

- 20

(1 mg/kg, i.p.)

IS

(p<0.01)

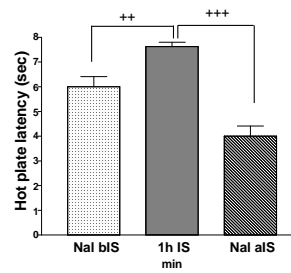
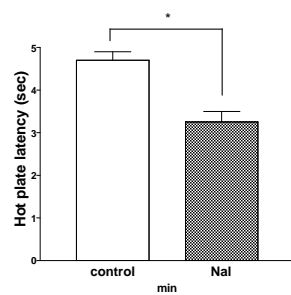
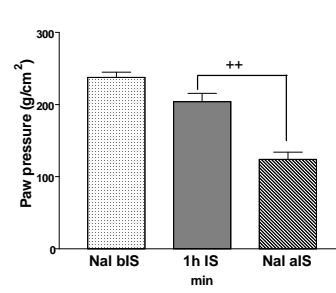
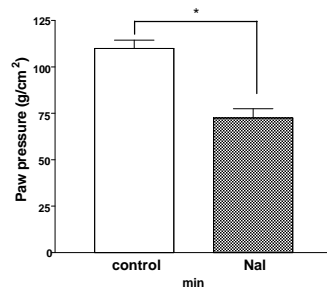
(p<0.001)

20

Nal.

IS

(p<0.01) (. 9 9).



.9.

(Nal),
Nal (1 mg/kg, i.p.)

(Nal bis)

(IS)

(Nal aIS)

()

() HP

;

È S.E.M.; *P<0.05

;

+P<0.05, ++P<0.01, +++P<0.001 1h IS.

SIA,

(Pacák K, Palkovits, 2001; Lapo, et al., 2003; Bocheva & Dzambazova, 2008a).

MIF-1 Tyr-Cav-MIF-1 - . Tyr-Cit-
 1 mg/kg, i.p. 20
 . 15
 .
 , (Nal)
 (IS) 20 Tyr-Cit-MIF-1 Tyr-Cav-MIF-1
 IS
 - .
 (.5 6).
 - -
 Nal+Tyr-Cit-MIF-1(<0.01) Nal+Tyr-Cav-MIF-1(<0.01)
 IS (.7 8).
 Tyr-Cit-MIF-
 1 Tyr-Cav-MIF-1 -
 MB+Tyr-Cit-MIF-1
 15 . (<0.05) 30 .
 (<0.05) IS Tyr-
 Cit-MIF-1 (.5).
 - 15
 . IS (<0.05)
 (.6).
 MB+Tyr-Cav-MIF-1
 15 . (<0.01), 30 (<0.01) 45 .
 (<0.01) IS (.7).
 - -
 - 15 (<0.01), 30 (<0.05) 45 . (<0.01)
 IS (.8).
 :
 ➤ Tyr-Cav-MIF-1 Tyr-Cit-MIF-1

- *Tyr-Cav-MIF-1* -
- Tyr-Cit-MIF-1.*
- *Tyr-Cav-MIF-1 Tyr-Cit-MIF-1* -
-
- IS
-
- IS
- *Tyr-Cav-MIF-1* -
- Tyr-Cit-MIF-1* -

MIF-1 Tyr-Cav-MIF-1 - Tyr-Cit-

(N) . A

(Vincent & Kimura, 1992; Yamada et al., 1995; Esch et al., 2002).

N ,

L-arginine N (Erchegui et al., 1992, 1993).

L-NAME (NO-) i.c.v. i.p.

(Erchegui et al., 1992; Esch et al., 2002).

L-arginine u SIN-1 ,

,

(Chung et al., 2003).

, NO ,

. 1997 .

, „ e ” ,

NO

,

NO,

(Moncada et al., 1997).

(Garthwaite, 1991; Snyder and Bredt, 1992).

SIA (Vincent & Kimura, 1992; Yamada et al., 1995; Esch et al., 2002).

NO (Costa (2005)).

NO

NO NA

(Esch T. et al., 2002). NO

(Gilinsky, M. et al., 2003).

L-NAME (10 mg/kg, i.p) L-Arg (1 mg/kg, i.p)

20

15

Tyr-Cit-MIF-1 Tyr-Cav-MIF-1 (1 mg/kg).

L-NAME+Tyr-Cit-MIF-1

15 (<0.01) 30

(<0.01)

15 (<0.01) IS (.10 11).

L-NAME+Tyr-Cav-MIF-1 15 (<0.01)

30

(<0.01)

15 (<0.05)

IS (.12 13).

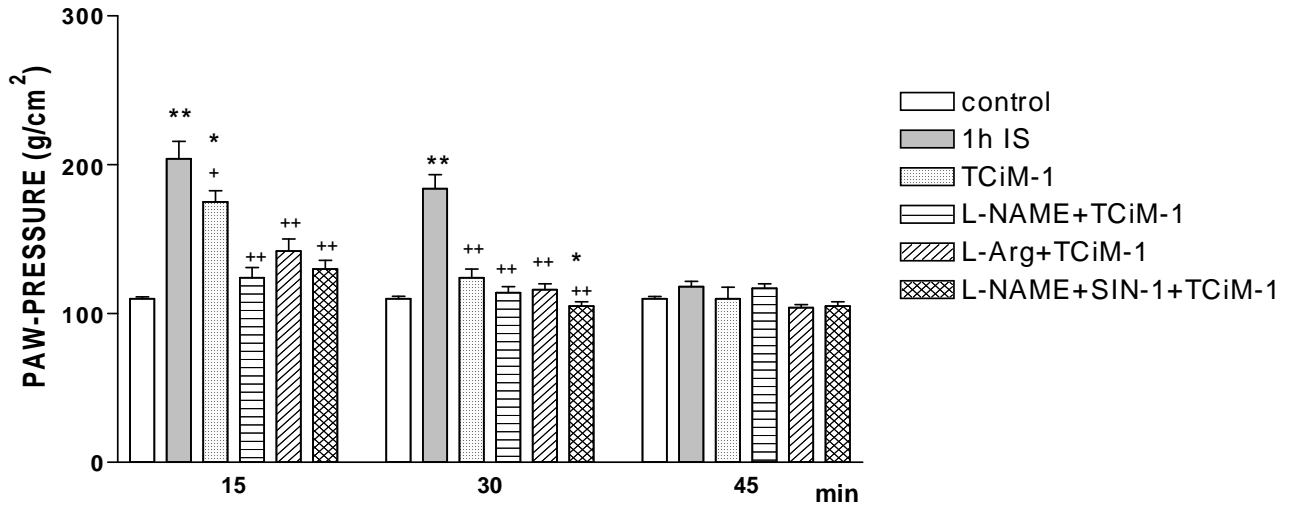
L-NAME, Tyr-Cav-MIF-1

15

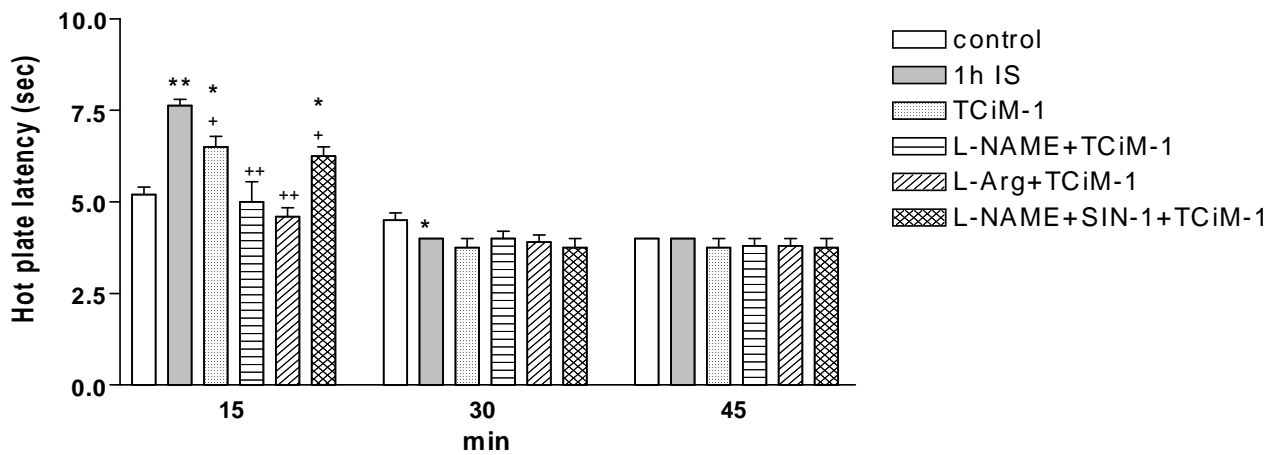
30 Tyr-Cav-MIF-1

Cit-MIF-1 - L-NAME+Tyr-Cav-MIF-1 L-NAME+Tyr-
 Cav-MIF-1. 30 Tyr-
 , L-arginine (L-arg)
 (i.c.v.) (s.c.) -
 (Erchegui et al., 1992, 1993; Esch et al., 2002).
 -
 L-arg (Esch et al., 2002).
 L-arginine (1 mg/kg, i.p.).
 L-arg+Tyr-Cit-MIF-1
 (<0.01)
 - (<0.01) 15 .
 IS (.10 11).
 L-arg+Tyr-Cav-MIF-1
 -
 (<0.01) 15 30 .
 IS, - 15 .
 IS (<0.01) (.12 13).
 L-Arg+Tyr-Cav-MIF-1 -
 IS L-Arg+Tyr-Cit-MIF-1.
 , SIN-1
 (Erchegyi et al., 1993). ethylene blue
 SIN-1, L-Arg-NO . ,
 μ- (Erchegyi et al., 1992).
 L-NAME+SIN-1+Tyr-Cit-MIF-1
 (<0.01) 15
 30 . - (<0.01) 15 .
 IS (.10 11).
 L-NAME+SIN-1+Tyr-Cav-MIF-1
 -
 (<0.01) 15 30 .

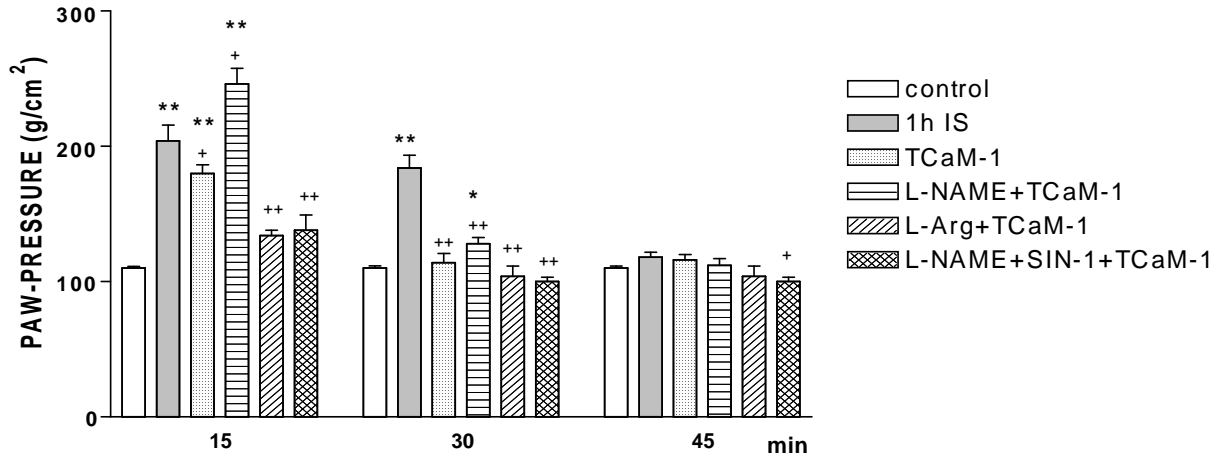
IS, - -
 15 . IS (<0.01) (.12 13).
 L-Arg+SIN-1+Tyr-Cav-MIF-1
 - L-Arg+SIN-1+Tyr-Cit-MIF-1.



. 10. Tyr-Cit-MIF-1 (1 mg/kg, i.p.) L-NAME (10 mg/kg, i.p.), L-Arg (1 mg/kg, i.p.) L-NAME+SIN-1 (SIN-1 - 0,2 mg/kg, i.p.)
 (1h IS) PP .
 *P<0.05; **P<0.01 ; *P<0.05, **P<0.01 1h IS. È S.E.M.;

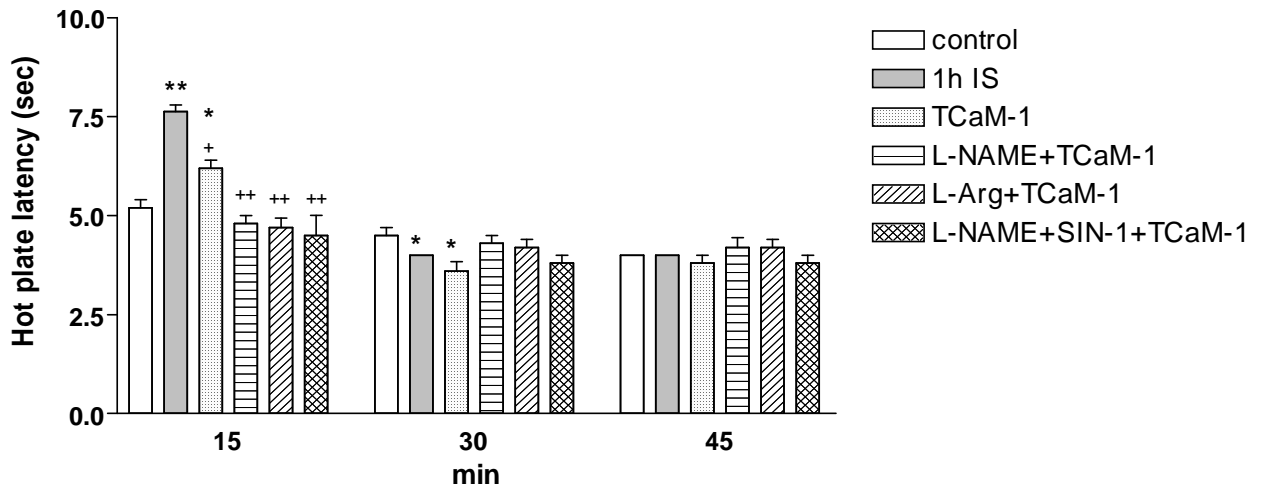


.11. Tyr-Cit-MIF-1 (i -1, 1 mg/kg, i.p.) L-NAME (10 mg/kg, i.p.), L-Arg (1 mg/kg, i.p.) L-NAME+SIN-1 (SIN-1 - 0,2 mg/kg, i.p.)
 (1h IS) HP .
 *P<0.05; **P<0.01 ; *P<0.05, **P<0.01 1h IS. È S.E.M.;



12. Tyr-Cav-MIF-1 (TCaM-1, 1 mg/kg, i.p.)
 mg/kg, i.p.), L-Arg (1 mg/kg, i.p.) L-NAME+SIN-1 (SIN-1 - 0,2 mg/kg, i.p.)
 (1h IS) PP .
 *P<0.05, **P<0.01 ; +P<0.05; ++P<0.01 1h IS.

L-NAME (10
 -
 S.E.M.;



13. Tyr-Cav-MIF-1 (TCaM-1, 1 mg/kg, i.p.)
 mg/kg, i.p.), L-Arg (1 mg/kg, i.p.) L-NAME+SIN-1 (SIN-1 - 0,2 mg/kg, i.p.)
 (1h IS) HP .
 *P<0.05; **P<0.01 ; ++P<0.01 1h IS.

L-NAME (10
 -
 S.E.M.;

:
 ➤ Tyr-Cit-MIF-1 Tyr-Cav-MIF-1 -
 ➤ Tyr-Cav-MIF-1 -
 L-NAME, L-Arg SIN-1

III.

Tyr-Cit-MIF-1, Tyr-Cav-MIF-1

(Galina & Kastin 1987; Kavaliers, 1988).

(Kavaliers, 1988), (Vaswani K. et al., 1988).

Tyr-Cit-MIF-1 Tyr-Cav-MIF-1

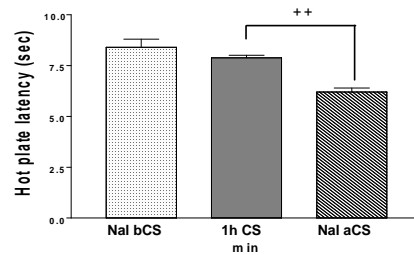
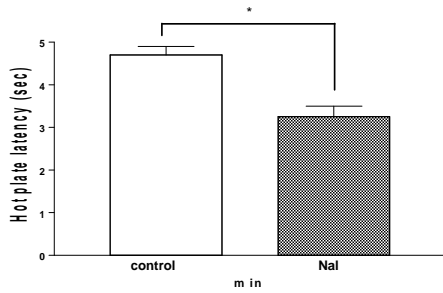
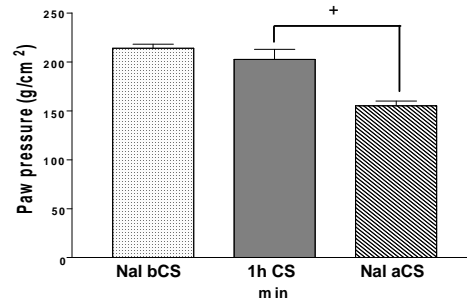
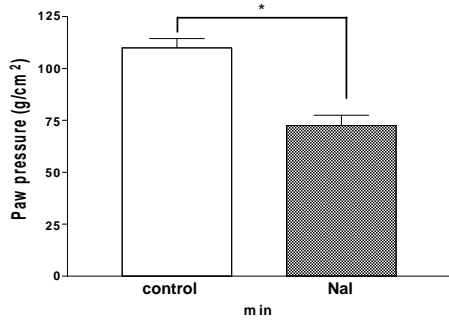
1 ml/kg, i.p. i.p. 1mg/kg 15

(1h CS), 15 (<0.01), 30 (<0.01) 45 (<0.05) ($> .15$).

(<0.01) 15 30 ($> .18$).

Nal 1h CS (p <0.01) ($> .14$ 14).

Tyr-Cit-MIF-1 (<0.05) ($> .15$).



. 14. (Nal), (CS) () () HP ;
 Nal (1 mg/kg, i.p.) (Nal bCS) (Nal aCS) ; +P<0.05, ++P<0.01, +++P<0.001
 S.E.M.; *P<0.05

1h CS.

Tyr-Cav-MIF-1

15 (<0.05), 30 (<0.01),
 45 (<0.05) (.17).

Tyr-Cav-MIF-1

(<0.01)(.18).

Nal+Tyr-Cit-MIF-1 (<0.01) Nal+Tyr-Cav-MIF-1

(<0.01)

(.15- 18).

CSIA (Kavaliers, 1988), , Nal

CS

(Vaswani K et al., 1988).

SIA, Nal

1 mg/kg, i.p.

- 20

Nal.

CS
(Galina & Kastin 1987; Kavaliers, 1988).

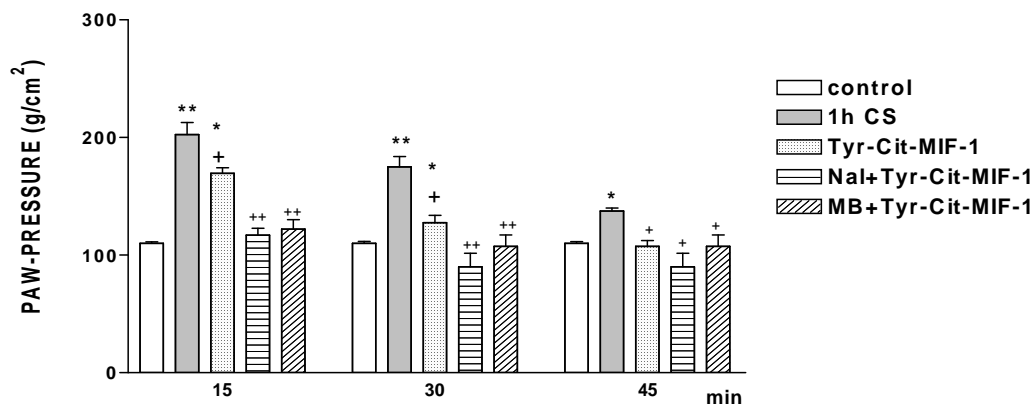
tail-flick hot-plate

MIF-1 Tyr-Cav-MIF-1 - Tyr-Cit-
thylene blue (MB). cGMP-

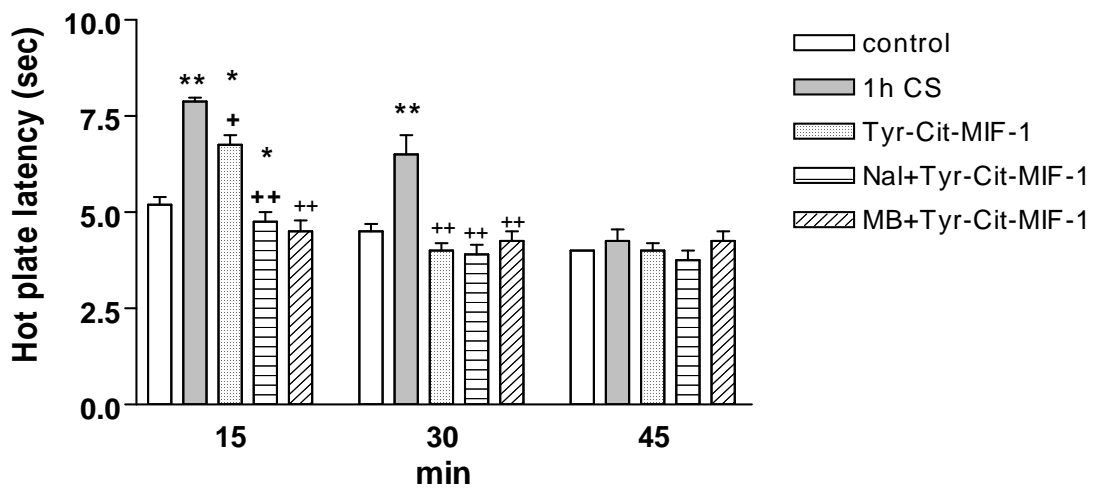
(Esch et al., 2002).

MB+Tyr-Cit-MIF-1 MB+Tyr-Cav-MIF-1

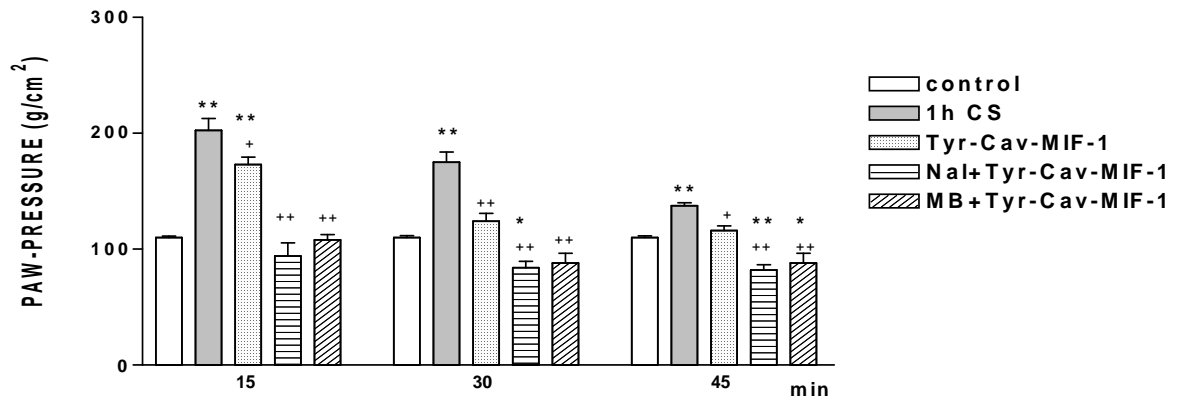
(. 15- 18).



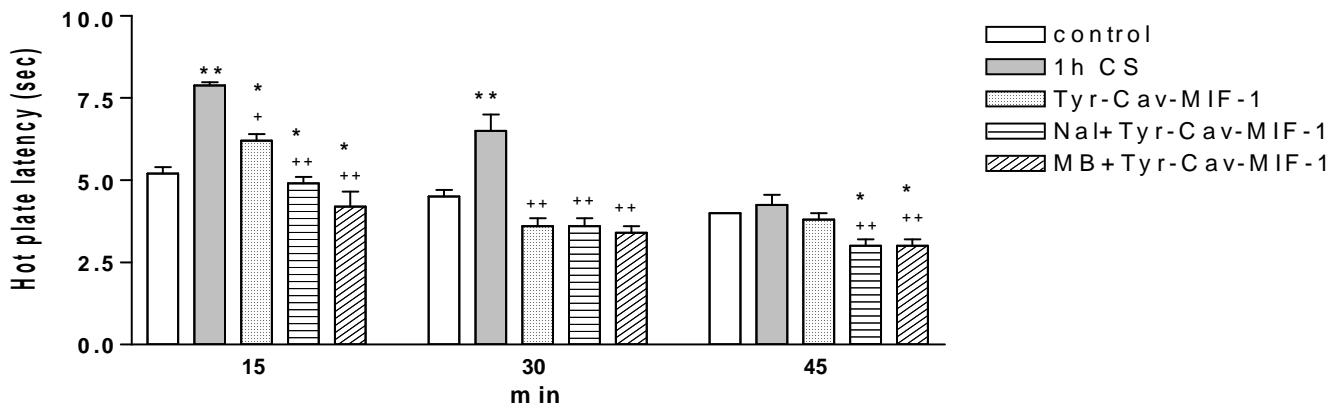
15. Tyr-Cit-MIF-1 (Nal)(1
mg/kg, i.p.) () (500µg/rat) - (1h CS) P
; +P<0.05, ++P<0.01 1h CS. S.E.M.; *P<0.05, **P<0.01



16. Tyr-Cit-MIF-1 (Nal)(1
mg/kg, i.p.) () (500µg/rat) - (1h CS) P
; +P<0.05, ++P<0.01 1h CS. S.E.M.; *P<0.05, **P<0.01



17. Tyr- -MIF-1 (500µg/rat) (Nal) (1 mg/kg, i.p.) (1h CS) P .
 S.E.M.; *P<0.05, **P<0.01 ;
 +P<0.05, ++P<0.01 1h CS.



18. Tyr-Cav-MIF-1 (500µg/rat) (Nal) (1 mg/kg, i.p.) (1h CS) P .
 S.E.M.; *P<0.05, **P<0.01 ;
 +P<0.05, ++P<0.01 1h CS.

➤ Tyr-Cit-MIF-1 Tyr-Cav-MIF-1 -

➤

➤ Tyr-Cav-MIF-1 -
 Tyr-Cit-MIF-1.

➤ , MB+Tyr-Cit-MIF-

1 MB+Tyr-Cav-MIF-1

Cav-MIF-1

Tyr-

Tyr-Cit-

MIF-1 Tyr-Cav-MIF-1

L-NAME

10 mg/kg, i.p.

L-NAME+Tyr-Cit-MIF-1

15 (<0.01), 30 (<0.01) 45 . (<0.05) - (.19).

L-NAME+Tyr-Cit-MIF-1

15 (<0.01) 30 . (<0.01) (.20).

L-NAME+Tyr-Cav-MIF-1

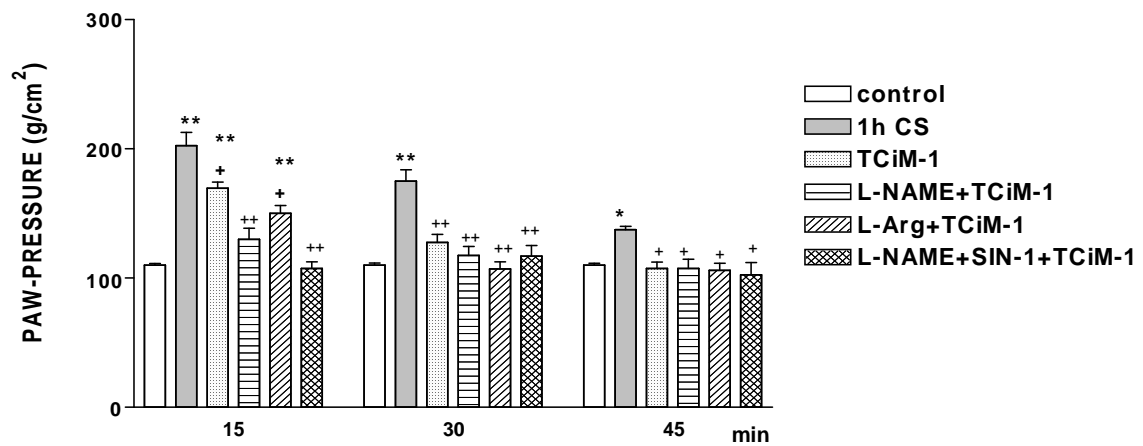
45 (<0.01)

S. 15 30 . L-NAME

(.21).

S

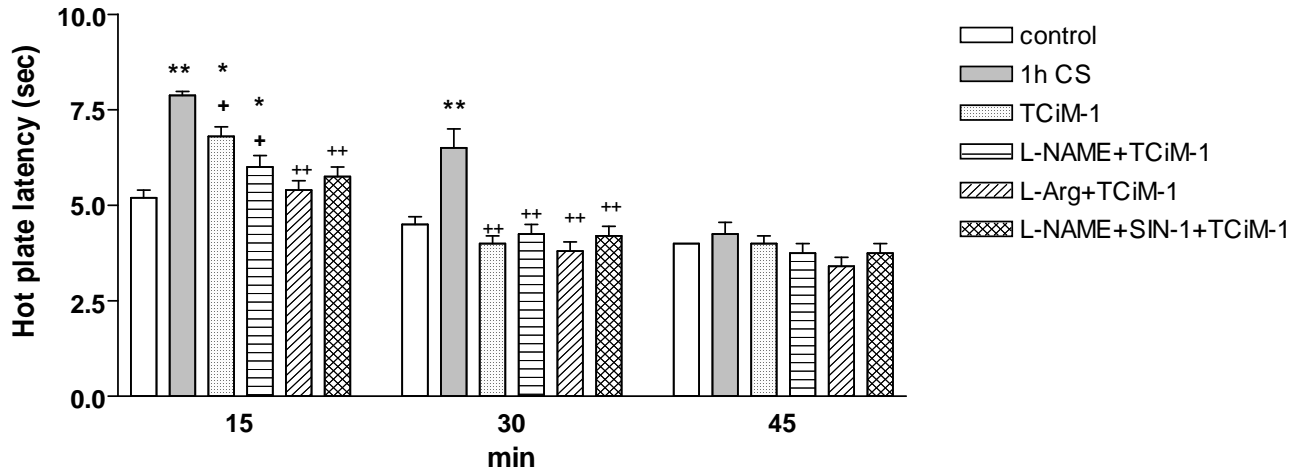
- 15 (<0.01), 30 (<0.01) 45 . (<0.05) (.22).



.19. Tyr-Cit-MIF-1 (TCiM-1, 1 mg/kg, i.p.)
 mg/kg, i.p.), L-Arg (1 mg/kg, i.p.) L-NAME+SIN-1 (SIN-1 - 0,2 mg/kg, i.p.)
 (1h S) PP .

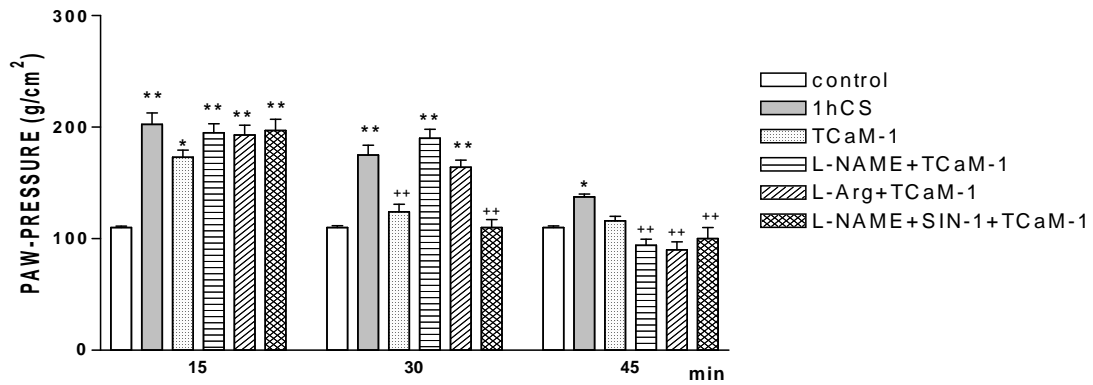
L-NAME (10
 -
 S.E.M.;

*P<0.05; **P<0.01 ; +P<0.05, ++P<0.01 1h S.



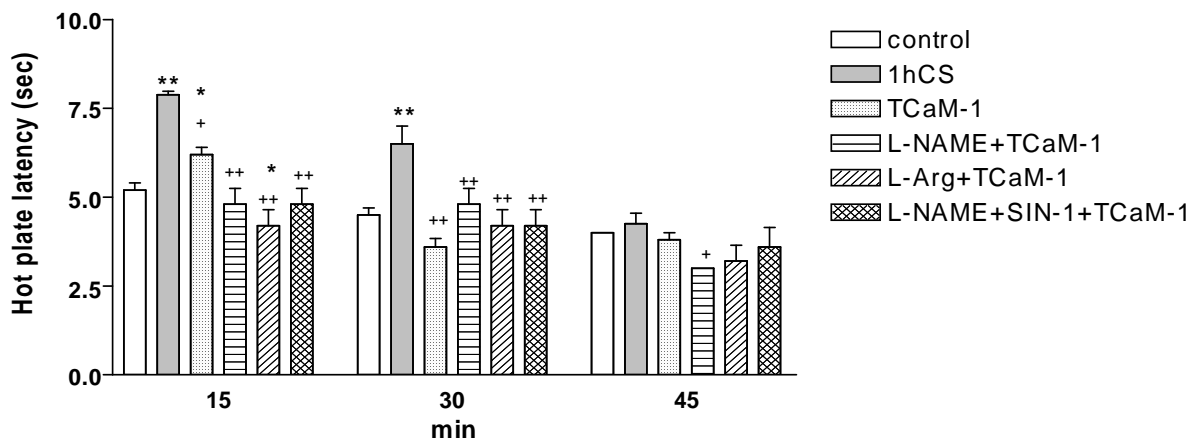
. 20. Tyr-Cit-MIF-1 (TCiM-1, 1 mg/kg, i.p.) L-NAME (10 mg/kg, i.p.), L-Arg (1 mg/kg, i.p.) L-NAME+SIN-1 (SIN-1 - 0,2 mg/kg, i.p.)
 (1h S) P . Ę S.E.M.;

*P<0.05; **P<0.01 ; +P<0.05, ++P<0.01 1h S.



. 21. Tyr-Cav-MIF-1 (TCaM-1, 1 mg/kg, i.p.) L-NAME (10 mg/kg, i.p.), L-Arg (1 mg/kg, i.p.) L-NAME+SIN-1 (SIN-1 - 0,2 mg/kg, i.p.)
 (1h S) PP . Ę S.E.M.;

*P<0.05; **P<0.01 ; +P<0.05, ++P<0.01 1h S.



. 22. Tyr-Cav-MIF-1 (TCaM-1, 1 mg/kg, i.p.) L-NAME (10mg/kg, i.p.), L-Arg (1 mg/kg, i.p.) L-NAME+SIN-1 (SIN-1 - 0,2 mg/kg, i.p.)
 (1h S) P . Ę S.E.M.;

*P<0.05; **P<0.01 ; +P<0.05, ++P<0.01 1h S.

L-arginine 1mg/kg, i.p.

L-arg+Tyr-Cit-MIF-1

(<0.01) (.19).

15 (<0.01) 30 . (<0.05)

S (.20).

L-arg+Tyr-Cav-MIF-1

15 (<0.01), 30 (<0.01)

45 . (<0.01)

15 (<0.01) 30 .

(<0.01)

S (.21 .22).

SIN-1

(0, 2 mg/kg, i.p.).

L-NAME+SIN-1+Tyr-Cit-MIF-1

15 (<0.01),

30 (<0.01) 45 . (<0.05)

15 (<0.01)

30 . (<0.01)

S (.19 .

20).

L-NAME+SIN-1+Tyr-Cav-MIF-1

30 45 .

(<0.01)

S,

-

-

15 30 .

S (<0.01) (.21 .22).

:

➤

, Tyr-Cit-MIF-1 Tyr-Cav-MIF-1

➤

➤

➤

Tyr-Cav-MIF-1

IV.

Tyr-Cit-MIF-1, Tyr-Cav-MIF-1

—

tail-flick hot-plate (Galina & Kastin 1987; Kavaliers, 1988).
 - (Kavaliers, 1988).

1ml/kg, i.p.

15 . (<0.01) ,
 30 (<0.05) 45 . (<0.01) (.
 23).
 -
 (. 24).

Tyr-Cit-MIF-1 Tyr-Cav-MIF-1 i.p. 1 mg/kg
 . 15
 , Tyr-Cit-MIF-1 (<0.01) 15 .
 - (. 23). -

Tyr-Cit-MIF-1 (. 24).
 Tyr-Cav-MIF-1
 - 15, 30 45 (<0.01)
 (. 25).
 - Tyr-Cav-MIF-1 -
 - 1
 (. 26).

MIF-1 Tyr-Cit-MIF-1 Tyr-Cav-
 - (.
 23 - 26).

20 1 S, . .

15 (<0.01), 30 (<0.05) 45 . (<0.01)

S (.23 .25).

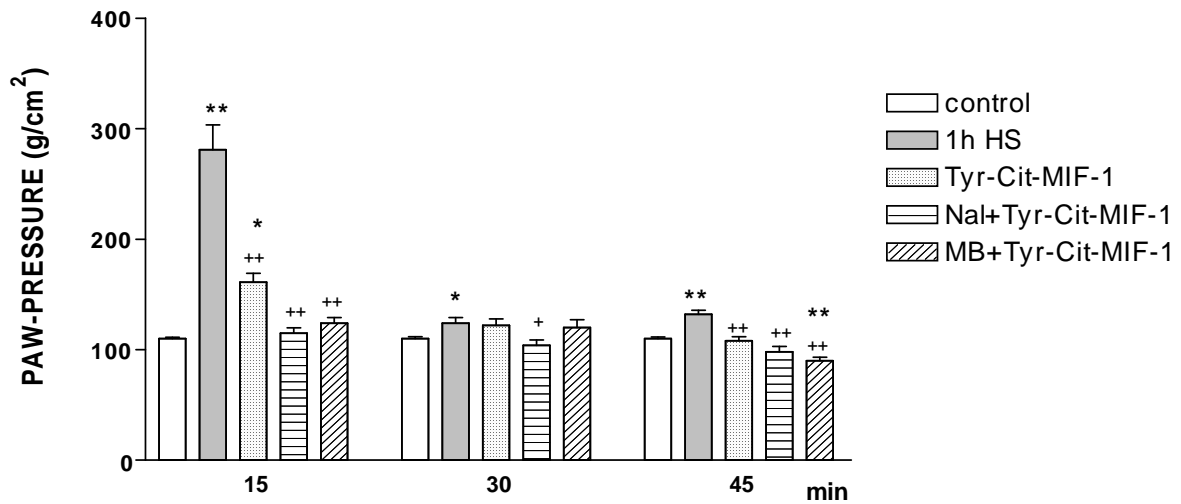
Nal+Tyr-Cit-MIF-1

Nal+Tyr-Cav-MIF-1

-

15, 30 45 .

S (.24 .26).



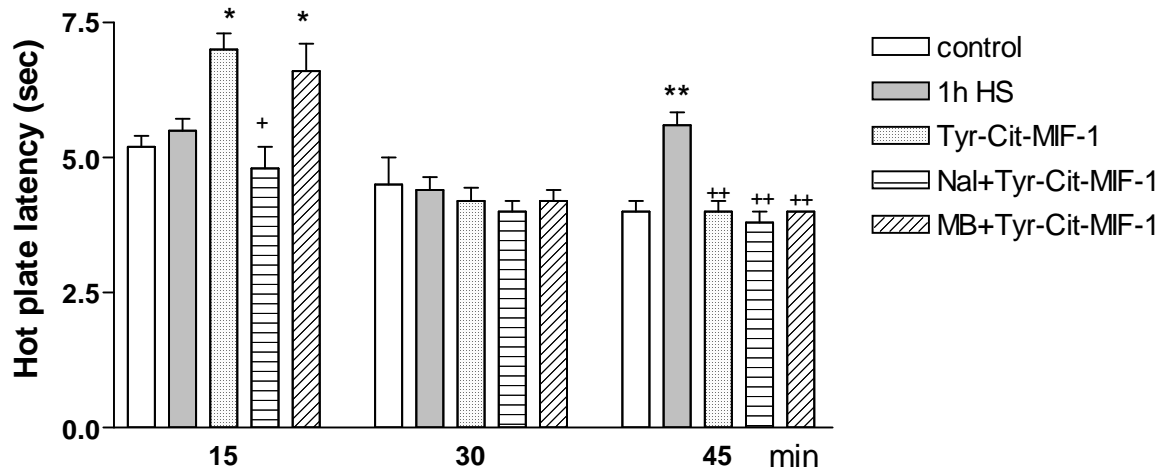
. 23.
mg/kg, i.p.)

Tyr-Cit-MIF-1
() (500µg/rat)

(Nal)(1
(1h S) P

È S.E.M.; *P<0.05, **P<0.01

; +P<0.05, ++P<0.01 1h S.



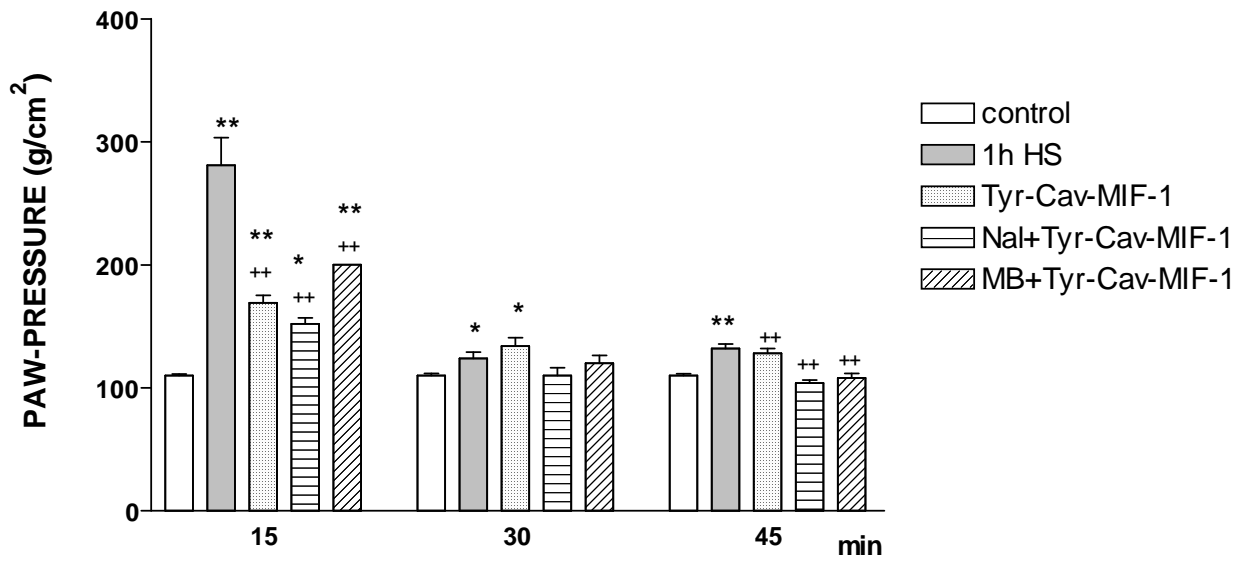
. 24.
mg/kg, i.p.)

Tyr-Cit-MIF-1
() (500µg/rat)

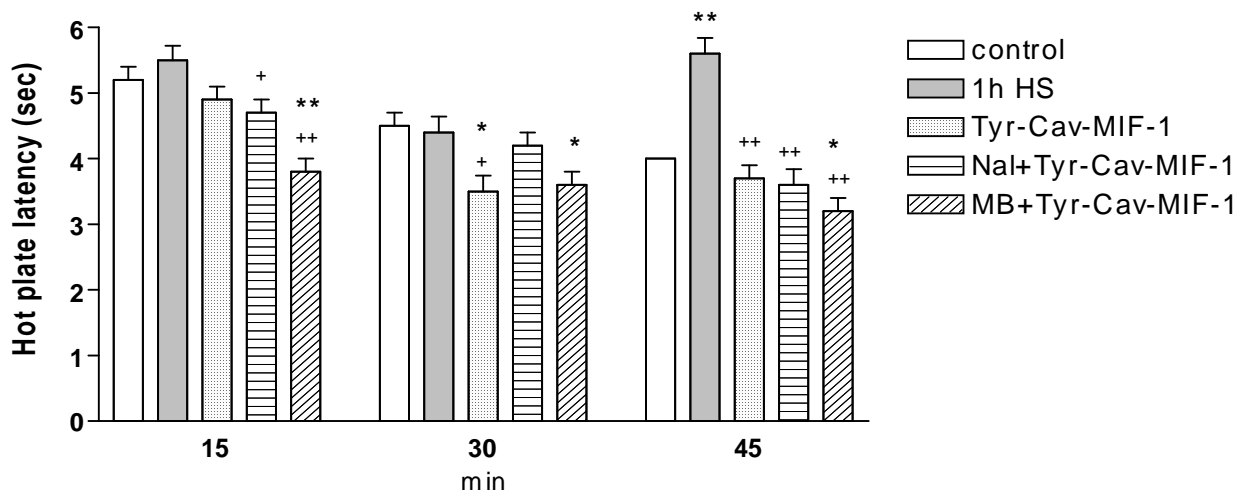
(Nal)(1
(1h S) P

È S.E.M.; *P<0.05, **P<0.01

; +P<0.05, ++P<0.01 1h S.



25. Tyr-Cav-MIF-1 (500µg/rat) (Nal) (1h S) 1 mg/kg, i.p. P
 S.E.M.; *P<0.05, **P<0.01
 ; *P<0.05, +P<0.05, ++P<0.01 1h S.

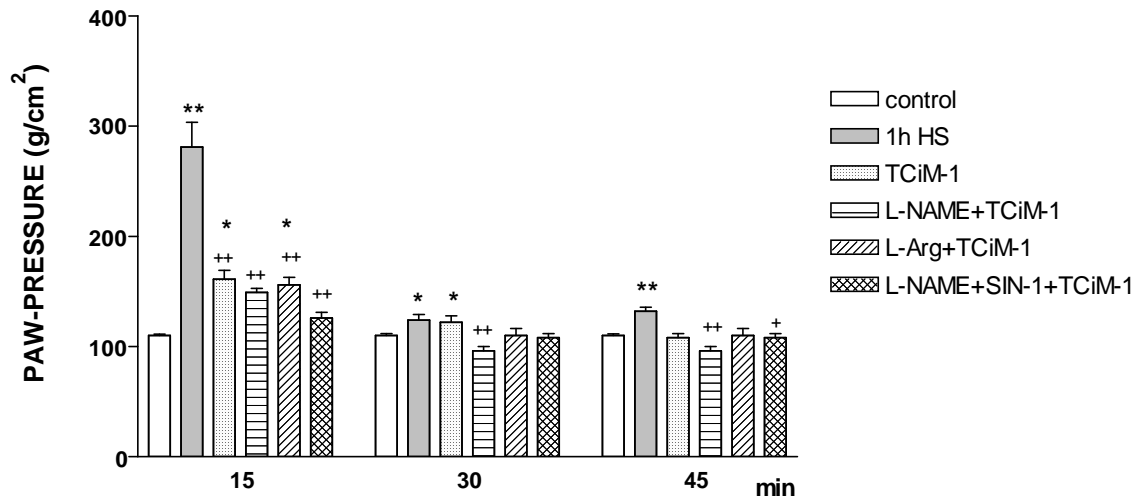


26. Tyr-MIF-1 (500µg/rat) (Nal) (1h S) 1 mg/kg, i.p. P
 S.E.M.; *P<0.05, **P<0.01
 +P<0.05, ++P<0.01 1h S.

➤ Tyr-Cit-MIF-1 Tyr-Cav-MIF-1

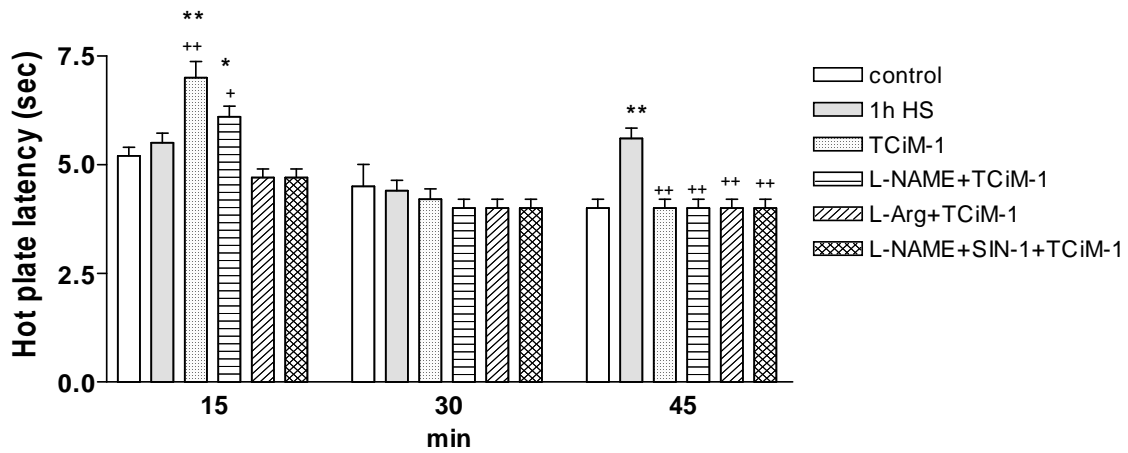
➤

Tyr-Cit-MIF-1 Tyr-Cav-MIF-1
 - .
 MB+Tyr-Cit-MIF-1
 15 (<0.01) 45 .
 (<0.01), - - 45 (<0.01)
 S (.23 .24).
 MB+Tyr-Cav-MIF-1
 - 15 (<0.01) 45
 . (<0.01), - (<0.01) (.25
 .26).
 :
 ,
 ➤ *Tyr-Cit-MIF-1 Tyr-Cav-MIF-1*
 ➤ - *Tyr-Cav-MIF-1*.
 Tyr-Cit-
 MIF-1 Tyr-Cav-MIF-1 - .
 - L-NAME
 10 mg/kg, i.p.
 L-NAME+Tyr-Cit-MIF-1
 -
 15 (<0.01), 30 (<0.01) 45 . (<0.01) (.27).
 L-NAME+Tyr- v-MIF-1
 30 (<0.01) 45
 (<0.01) S, 15 . L-NAME
 ,
 (.29).
 L-NAME Tyr-Cit-MIF-1 Tyr- v-MIF-1
 -
 - 45 . (<0.01) (.28 .30).



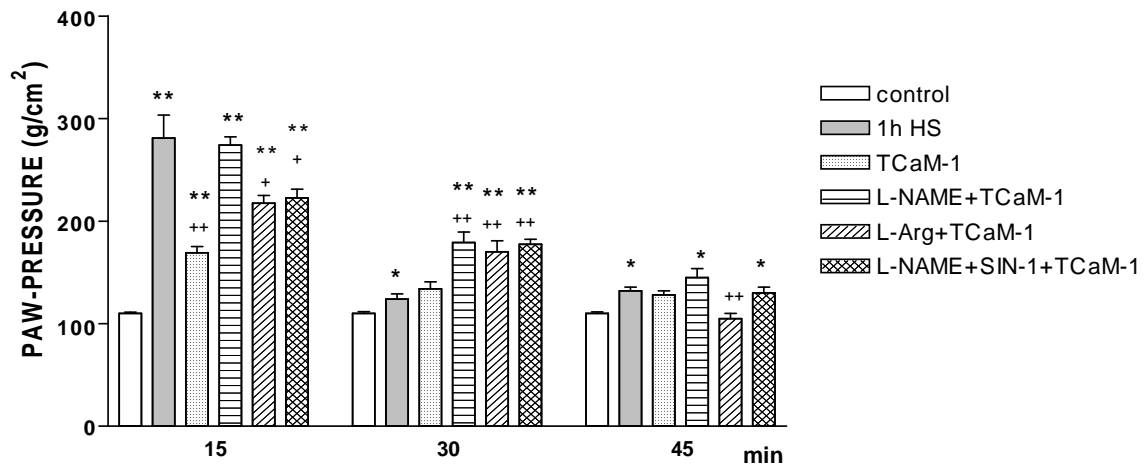
27. Tyr-Cit-MIF-1 (TCiM-1, 1 mg/kg, i.p.) L-NAME (10 mg/kg, i.p.), L-Arg (1 mg/kg, i.p.) L-NAME+SIN-1 (SIN-1 - 0,2 mg/kg, i.p.)
 (1h S) P . S.E.M.;

* $P < 0.05$; ** $P < 0.01$; + $P < 0.05$, ++ $P < 0.01$ 1h S.

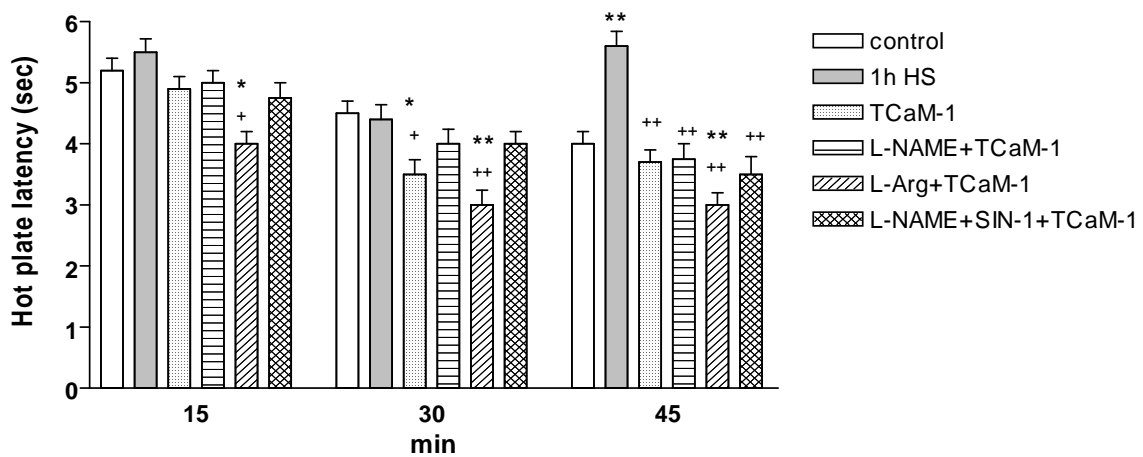


28. Tyr-Cit-MIF-1 (TCiM-1, 1 mg/kg, i.p.) L-NAME (10 mg/kg, i.p.), L-Arg (1 mg/kg, i.p.) L-NAME+SIN-1 (SIN-1 - 0,2 mg/kg, i.p.)
 (1h S) P . S.E.M.;

* $P < 0.05$; ** $P < 0.01$; + $P < 0.05$, ++ $P < 0.01$ 1h S.



29. Tyr-Cav-MIF-1 (TCaM-1, 1 mg/kg, i.p.) L-NAME (10 mg/kg, i.p.), L-Arg (1 mg/kg, i.p.) L-NAME+SIN-1 (SIN-1 - 0,2 mg/kg, i.p.)
 (1h S) PP . S.E.M.;
 *P<0.05; **P<0.01 ; +P<0.05, ++P<0.01 1h S.



30. Tyr-Cav-MIF-1 (TCaM-1, 1 mg/kg, i.p.) L-NAME (10mg/kg, i.p.), L-Arg (1 mg/kg, i.p.) L-NAME+SIN-1 (SIN-1 - 0,2 mg/kg, i.p.)
 (1h S) P . S.E.M.;
 *P<0.05; **P<0.01 ; +P<0.05, ++P<0.01 1h S.

L-arginine 1 mg/kg, i.p.
 L-arg+Tyr-Cit-MIF-1
 - 15 (<0.01) 45 . (<0.01)
 ,
 - S
 45 . (<0.01) (.27 .28).
 L-arg+Tyr-Cav-MIF-1
 -

(<0.01), 30 (<0.01) 45 . (<0.01)

(.28 .30).

SIN-1

0, 2 mg/kg, i.p.

L-NAME+SIN-1+Tyr-Cit-MIF-1

15 (<0.01) 45 .

(<0.05)

- 45 . (<0.01)

S (.27 .28).

L-NAME+SIN-1+Tyr-Cav-MIF-1

15 (<0.05),

30 . (<0.01) 45 . (<0.01)

S, - 45 . (<0.01)

S (.29 .30).

:

➤ , Tyr-Cit-MIF-1 Tyr-Cav-MIF-1

➤

➤

MIF-1 Tyr-Cav-MIF-1

Tyr-MIF-1.

Tyr-Cit-

M. Palkovits, 2001).

(NO)

/

(Sushko,B.S. & Yu. P. Limanskii,

2001). NO

NMDA

(Dickenson, A.H., 1995).

(hypothalamic-pituitary-adrenal - HPA)

(Gilinsky, M.A. et al., 2003; Uribe,

R.M. et al., 1999; Gupta, V. et al., A. 2005).

NO

IS.

(Von Bohlen und Halbach O. & R. Dermietzel, 2007).

IS, CS

HS

μ-

NO μ-
NO

Tyr-Cit-MIF-1 Tyr-Cav-MIF-1

μ-

(Pacak, K. & M. Palkovits, 2001).

Tyr-Cit-MIF-1 Tyr-Cav-

MIF-1

V.
Tyr-Cav-MIF-1
(PAG)

Tyr-Cit-MIF-1

TA

(NOS)

PERIAQUEDUCTAL GRAY

(Lapo et al., 2003; Von Bohlen und Halbach & R. Dermietzel., 2007).

(hypothalamo-pituitary-adrenal - HPA)

(Yuksel, S.& Yurekli, M., 2003).

(NO)

HPA

(Uribe, R. et al., 1999).

(Gilinsky, M. et al., 2003).

Tyr-Cit-MIF-1

Tyr-Cav-MIF-1

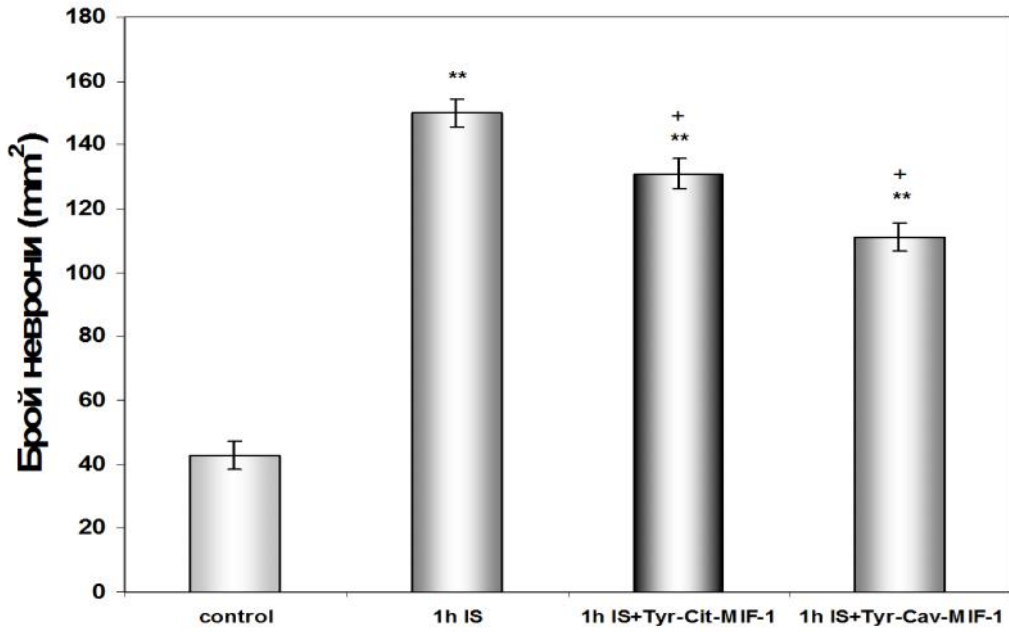
periaqueductal gray (PAG) –

PAG

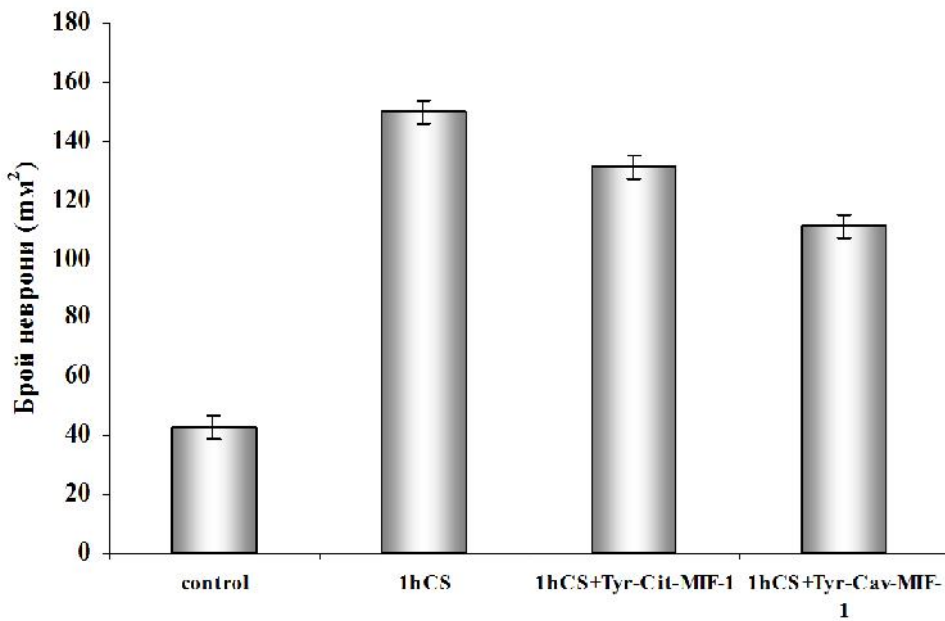
Wistar (180-200g).

Tyr-Cit-MIF-1 Tyr-Cav-MIF-1

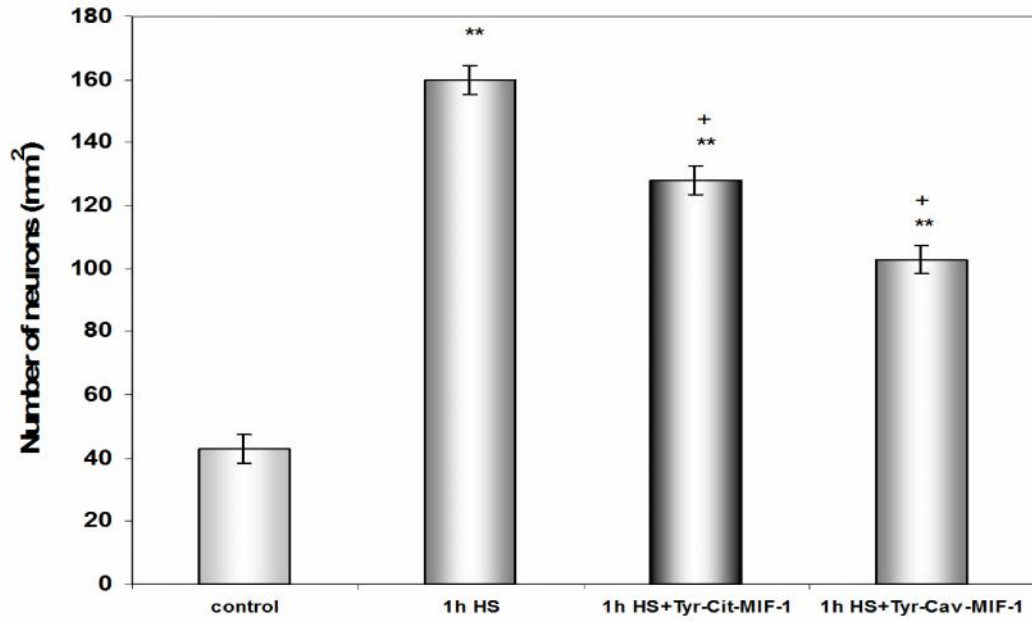
15



. 31. Tyr-Cit-MIF-1 Tyr-Cav-MIF-1 NOS PAG
(1h IS).
± S.E.M.; *P<0.01, +++P<0.001 ; **P<0.05



. 32. Tyr-Cit-MIF-1 Tyr-Cav-MIF-1 NOS PAG
(1h S).
± S.E.M.; *P<0.01, +++P<0.001 ; **P<0.05



. 33. *Tyr-Cit-MIF-1* *Tyr-Cav-MIF-1* *NOS* *PAG*
 (1h S). ± S.E.M.;
 P*<0.01, +++*P*<0.001 ; *P*<0.05

, ,
 NOS PAG
 . *Tyr-Cit-MIF-1* *Tyr-Cav-MIF-1* 1h IS, 1h S 1h S
 NOS PAG , *Tyr-Cav-MIF-1* -
Tyr-Cit-MIF-1.

() (Pacák & Palkovits, 2001).
(de Kloet, 2003; Tsigos et al., 2004; Armario, 2006).

(Riedel, 2000).
(Riedel, 2000).
Tyr-MIF-1 MIF-1, Tyr-MIF-1,
Tyr-W-MIF-1 Tyr- -MIF-1
(AOP) (Cesselin F., 1995).

μ-
Tyr-Cit-MIF-1 Tyr-Cav-MIF-1
Tyr-MIF-1 -
Tyr-Cav-MIF-1 Tyr-Cit-MIF-1 -

– () ().

.

NADPH-d PAG ,
Tyr-Cav-MIF-1 Tyr-Cit-MIF-1.

- .
(1mg/kg,).

- .
, Tyr-Cav-MIF-1
Tyr-Cit-MIF-1 , - Tyr-MIF-1.
- Tyr-Cav-MIF-1.
L-canavanine, L-ornitine, L-citruline
, L-canaline (Bocheva et
al.,2001).

,

,

(Rosenthal et al, 1975).

-
NH₃ .
, NH₃ 2 .
-

, -
, NOS. A - N-hydrohyl-
arginine, (Cit)

.

,

,
L- ,
(Coenen et al., 2007).

L-canavanine, L-arginine, L-ornithine, L-citrulline L-
canaline.

L-canaline,
(Dzambazova-Maximova et al, 2003, 2005).

L-canavanine
MIF-1
(Bocheva et al, 2003, 2008 a, b; Boyanov et al,
2005).

(Miczek et al., 1982; Teskey et al., 1984; Lester
& Fanselow, 1985; Kavaliers & Innes, 1987; Kavaliers, 1990; Kavaliers & Colwell, 1991).

(Amir & Amit, 1978;
Appelbaum & Holtzman, 1985; Aloisi et al., 1998; Galina & Kastin 1987; Kavaliers, 1987).

(Inoe et al., 2003).

(Tanaka et al., 1985, 1988).

Tyr-Cav-MIF-1 Tyr-Cit-MIF-1

Tyr-Cav-MIF-1 Tyr-Cit-MIF-1

M. Palkovits, 2001).

(Pacak, K. &

(Pacák and Palkovits, 2001).

1982 .

Tyr-MIF-1 (Zadina et al., 1992).

Tyr-MIF-1

, Tyr-MIF-1

(Zadina et al., 1994).

Tyr-MIF-1

Tyr-MIF-1

(Banks and Kastin, 1984; Banks et al., 1987; Banks et al., 1990; Banks and Kastin, 1994;).

(Miczek et al., 1982; Teskey et al., 1984; Lester &

Fanselow, 1985; Kavaliers & Innes, 1987; Kavaliers, 1990; Kavaliers & Colwell, 1991).

SIA,

Tyr-Cav-MIF-1 Tyr-Cit-MIF-1

, Nal tail-flick hot-plate
 (Amir Amit, 1978).
 , Nal
 (Kiyatkin E.A., 1989).
 Nal CSIA (Kavaliers, 1987),
 CS Nal - (Vaswani K et al., 1987).
 , Nal
 , SIA
 (Vaswani et al., 1988; Tsuda et al., 1989; Inoe et al., 2003)
 , (Tsuda et al., 1989; Pacák K, Palkovits, 2001;
 Inoe et al., 2003; Lapo, et al., 2003).
 / SIA.
 , - , (Pacák
 K, Palkovits, 2001; Bocheva & Dzambazova, 2008a).
 , Nal
 Tyr-Cav-MIF-1 Tyr-Cit-MIF-1
 , NO-
 Tyr-Cav-MIF-1 Tyr-Cit-MIF-1.
 Tyr-Cav-MIF-1 Tyr-Cit-MIF-1,
 L-NAME L-
 Arg Tyr-Cav-MIF-1 Tyr-Cit-MIF-1,
 (hypothalamic-pituitary-adrenal - HPA) .

(Gilinsky, M.A. et al., 2003; Uribe, R.M. et al., 1999; Gupta, V. et al., A. 2005).

, NO
IS (Gupta, V. et al., A. 2005).

(Von Bohlen und Halbach O. & R. Dermietzel, 2007).

,
μ-
.
.
.
.

Tyr-Cav-MIF-1 Tyr-Cit-MIF-1.

,
.
(Pacak, K. & M. Palkovits, 2001).

,
Tyr-Cit-MIF-1 Tyr-Cav-
MIF-1 -

(Garthwaite, 1991; Snyder and Bredt, 1992).

NMDA
, NO
(Mayer et al., 1999).

, N SIA (Yamada et al., 1995; Vincent & Kimura, 1992; Esch et al., 2002).
NO - (Gilinsky, M. et al., 2003).

NO SIA ,
 L-NAME, tail-
 flick ISIA (H ulic et al., 1997).
 NO ,
 NO NO NA
 (Esch T. et al., 2002).
 NMDA
 NO (Riedel W., 2000).
 IL-1
 CR NO - NO
 NMDA
 CR NO.
 Tyr-MIF-1
 Tyr-MIF-1- , -
 (Banks and Kastin, 1994). Tyr-
 MIF-1
 Tyr-MIF-1 t- (Banks and Kastin, 1994).
 (Horvath
 et Kastin, 1990) (Horvath et Kastin, 1989). Tyr-MIF-1
in vivo in vitro (Kastin et al., 1994).
 Tyr-MIF-1
 (Zamfirova, Bocheva et al., 2003., Bocheva et
 al. 2004). Tyr-MIF-1
 Tyr-MIF-1 -
 (Bocheva & Dzambazova,
 2004a; Bocheva & Dzambazova, 2004b).

nNOS NADPH-d (Wolf, 1997).

G

nNOS (Bredt et al., 1990)
NADPH-d (Hatakeyama et al., 1996; Krukoff & Khalili, 1997;
Shirakawa et al., 2004) , nNOS G
- , Tyr-MIF-1
(Vincent & Kimura, 1992; Calzà et al., 1993; Kishimoto et al., 1996; McLeod et al., 2001;
Hori et al., 2005).

nNOS (McCann et al., 1996)
(Thorns et al., 1998).

nNOS NADPH-d
G , .
, ,
nNOS NADPH-d G
, NO .
, NO, NOS (McLeod
et al., 2001; Masood et al., 2004). , NO
HPA (Uribe, R. et al., 1999).

, IS nNOS- G NO
HPA (Calzà et al., 1993; Hatakeyama et al., 1996;
Kishimoto et al., 1996; Krukoff & Khalili, 1997; Hori et al., 2004).

CR NO (Gotti et al., 2005).
Tyr-Cav-MIF-1 Tyr-Cit-MIF-1 ,
nNOS NADPH-d
G .
Tyr-Cav-MIF-1 - Tyr-Cit-MIF-1.
, NO G (Uribe R.M., et al., 1999;
Gilinsky M.A. et al., 2003; Gupta V. et al., 2005).

, NO, -
NMDA CRH-

RH -

(Antoni, 1986; Johnson et al., 1992; Dallman, 1993; Cullinan et al., 1995; Peñalva, 2002).

- - ,
(Martin R. & Voigt

K., 1981; Watson S. et al., 1982).

- Tyr-Cav-MIF-1 - , Cav

- NO

CR -

NO

Tyr-Cav-MIF-1 Tyr-Cit-MIF-

1

- NMDA ,

,

1. e ,
;
2. Tyr-Cav-MIF-1 Tyr-Cit-MIF-1 -
;
3. Tyr-Cav-MIF-1 Tyr-Cit-MIF-1 ,
SI ;
4. Tyr-Cav-MIF-1 Tyr-Cit-MIF-1
, SI ,
;
5. L-NAME, SIN-1 L-Arg Tyr-Cav-MIF-1 Tyr-Cit-MIF-1
,
- ,
;
6. NADPH-d- nNOS PAG
.
7. Tyr-Cit-MIF-1 Tyr-Cav-MIF-1
NADPH-d- ,
nNOS PAG. Tyr-Cav-MIF-1 - Tyr-
Cit-MIF-1.
8. *in vivo in vitro*
.

- ,
1. Tyr-MIF-1
Tyr-Cav-MIF-1 Tyr-Cit-MIF-1
Tyr-MIF-1.
 2. Tyr-Cav-MIF-1 Tyr-Cit-MIF-1 -
L-canavanine L-citruline.
 3. Tyr-Cav-MIF-1 Tyr-Cit-MIF-1 ,
- ;
 4. Tyr-Cav-MIF-1 Tyr-Cit-MIF-1 ,
 5. Tyr-Cav-MIF-1 Tyr-Cit-MIF-1
NADPH-d- nNOS PAG ;

1. " " - -04/2005 . : " Tyr-MIF-1: - " 2. 21/2010 , : " 1 periaqueductal gr y " . 3. 23 /2011 . : " Tyr-W-MIF-1 Tyr-K-MIF-1 1- periaqueductal gr y " .

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3. **Hadjiolova R.K.**, E.B. Dzambazova, B.V. Landzhov, A.I. Bocheva, A.B. Bozhilova-Pastirova. Influence of newly synthesized Tyr-MIF-1's analogues on nitric oxide synthase and tyrosine hydroxylase expression in rat's periaqueductal gray after immobilization stress. **J Biomed Clin Res**, **2(2), 77-81, 2010.**
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