

ACTH

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The effect of quercetin (from onion) and ACTH on morphine induced tolerance and dependence in mice

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Objectives: The goal of this study was to evaluate the effects of ACTH and Quercetin on preventing the development of morphine tolerance and dependence in mice. **Methods:** In this study different groups of mice (20-30 g) received morphine (40 mg/kg, ip) , morphine (40 mg/kg, ip) + ACTH (1,2.5,5 IU/mice, ip), morphine (40 mg/kg, ip) + Quercetin (5,10,25 mg/kg, ip), morphine (40 mg/kg, ip) + Quercetin (5mg/kg, ip)+ ACTH (1 IU/mice, ip)] once a day for four days. Tolerance was assessed by administration of morphine (9 mg/kg, ip) and using hot plate test on fifth day. Withdrawal symptoms were assessed by administration of naloxone (4 mg/kg, ip) two hours after co-administration of morphine with either Quercetin or ACTH. **Results:** It was found that pretreatment with Quercetin or ACTH decreased the degree of tolerance and dependence significantly. Additionally, co-administration of Quercetin and ACTH before morphine administration decreased significantly the tolerance and dependency. From these results it may be concluded that administration of Quercetin or ACTH injection alone or in together could affect the decrease withdrawal signs and tolerance of morphine. These effects may be related to as nitric oxide inhibitor (NOI) behavior of Quercetin and the ability of Morphine and their receptors in the control of the secretion of CRH. **Conclusion:** ACTH, quercetin and co-administration of both drugs significantly inhibited the development of morphine induced tolerance and dependence in mice.

Key words: ACTH, Quercetin , Morphine , Tolerance, Withdrawal.

ACTH (NO)

+ (mg/kg,ip) (mg/kg,ip)

+ (mg/kg,ip) (mg/kg,ip) + (mg/kg,ip) (/ IU/mice,ip) ACTH

(mg/kg,ip) + (IU/mice,ip) ACTH

(mg/kg,ip)

ACTH : () () Hot-plate

ACTH : (P< /)

ACTH : (P< /)

ACTH :

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ACTH ()

ACTH

ACTH ()

(- Novartis Pharma AG) ACTH •

() DMSO •

(-) •

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() Silicagel 60 F₂₅₄ •

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%

NMDA

(.)

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(.)

(ACTH)

(/)

ACTH

(CRH)

(mg/kg,ip) () (Vacuum Liquid Chromatography) VLC ()

(Jumping) VLC ()

(Standing on feet) (Thin Layer Chromatography) TLC (- -) - -

MeOH-d4 Silica gel GF254 HNMR MHz

Mean ± SE ()

ANOVA **Hot-plate** :

Tukey ±

p < / Hot-plate

(Latency time)

(mg/kg,ip) : (Cut off)

() (Tolerance) :

mg/kg,ip (mg/kg ,ip)

(ml/kg ,ip) DMSO %

(mg/kg,ip) ACTH (ml/kg ,ip) (DMSO)

(/ IU/mice,ip) ACTH

(IU/mice,ip) ACTH

DMSO % (mg/kg,ip)

(/ IU/mice,ip) ACTH ()

ACTH (mg/kg,ip)

ACTH (p < /) ()

() Hot-plate :

(mg/kg,ip) :

(mg/kg,ip) ()

ACTH (ml/kg ,ip) DMSO %

(mg/kg,ip) (/ IU/mice,ip)

(IU/mice,ip) ACTH

DMSO % (mg/kg,ip)

(p < /)

()

ACTH (/ IU/mice,ip) ACTH (IU/mice,ip) ACTH :
 (mg/kg,ip) (IU/mice,ip) (mg/kg,ip)
) (IU/mice,ip)ACTH ()
 (mg/kg,ip)

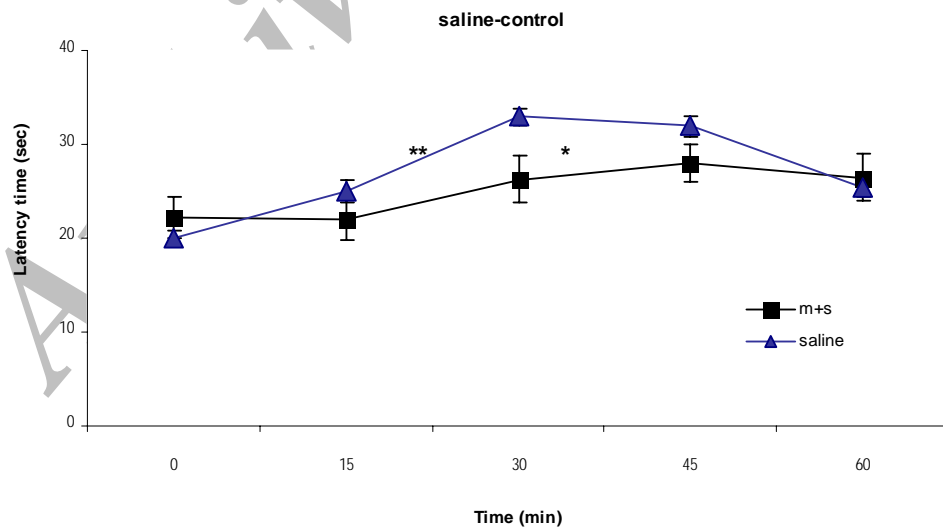
ACTH :

()

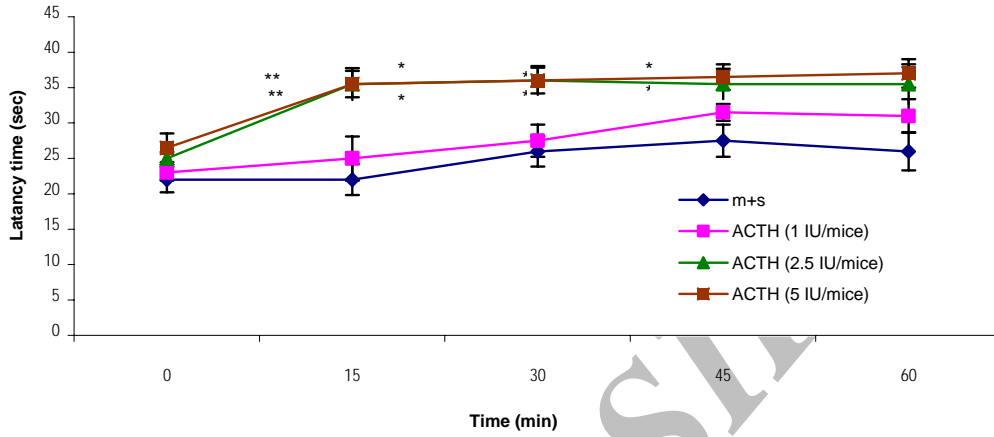
() ACTH .(p< /)

(/ IU/mice,ip) ACTH
 (mg/kg,ip)
 (mg/kg,ip) (IU/mice,ip)ACTH **ACTH** :

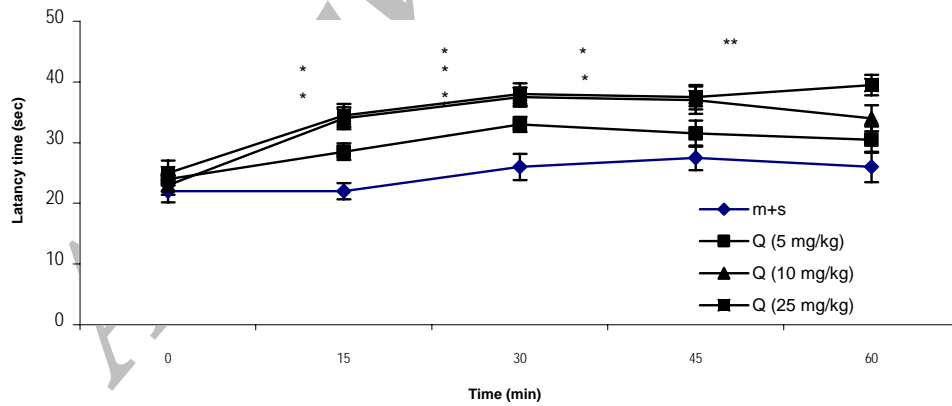
() ()
 .(p< /)



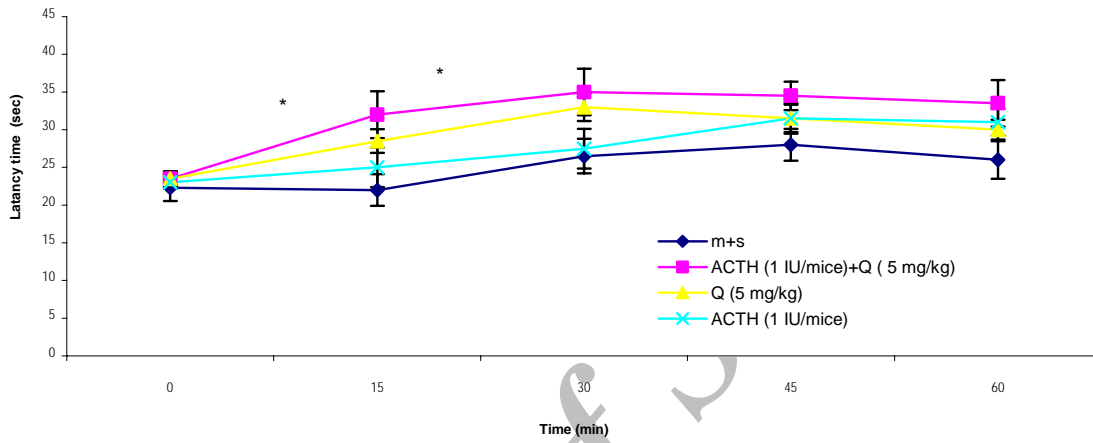
DMSO % :m
 (salin) (mg/kg,ip) :
 Mean±SE (m+s) (mg/kg,ip)
 () ** p< / * p< /



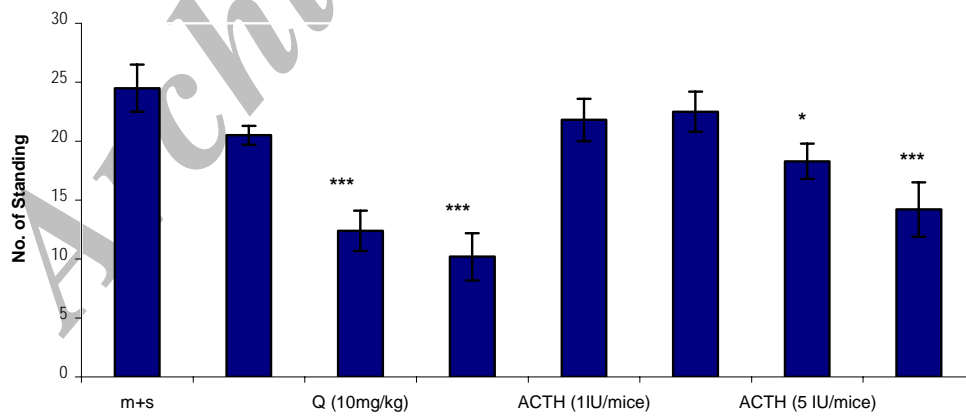
Mean±SE () DMSO % (/ IU/mice,ip) ACTH : ** p<0.01 , * p< 0.05



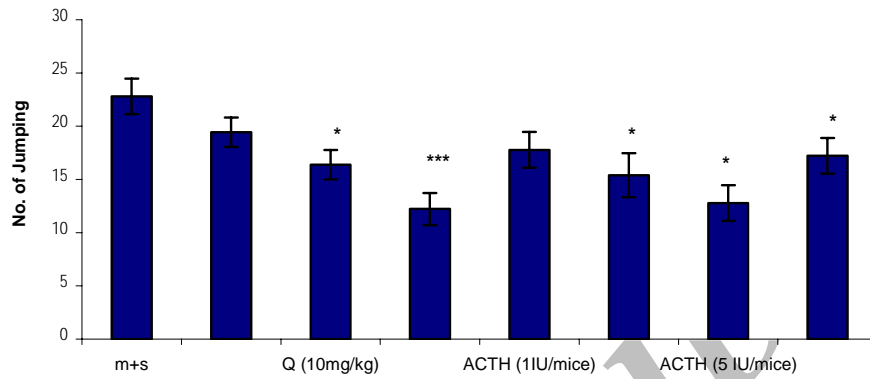
Mean±SE () DMSO % (/ mg/kg,ip) Q : ***p<0.001, ** p<0.01 , * p< 0.05



Mean±SE () :Q DMSO % (mg/kg,ip) :s :m (IU/mice,ip)ACTH : ** p<0.01 , * p< 0.05 .



:Q DMSO % (mg/kg,ip) :s :m (IU/mice,ip) ACTH : (mg/kg,ip) : Mean ±SE ***p<0.001, * p< 0.05



(IU/mice,ip) ACTH (mg/kg,ip) :Q DMSO % (/ IU/mice,ip) ACTH (mg/kg,ip) :
 Mean ±SE ***p<0.001, ** p<0.01, * p< 0.05

NMDA NO (NO μ () NMDA ()
 NMDA NO ACTH () (PKC) Protein Kinase A NMDA (Mg⁺⁺) NMDA ()
 (mg/kg,ip) () (p< /) () withdrawal ()
 () (p< /) Ca²⁺ () () PKC NO ()

() ()) NO
 (Jumping) PKC (NMDA
 . ()
 ACTH
 (P< /) (Standing on feet) (/ IU/mice,ip ACTH)
 (P< /)
 ACTH
 (Jumping) . ()
 ACTH
 CRH (Rat)
 () ACTH
 ACTH ACTH
 ACTH ACTH
 ACTH ACTH
 ACTH ACTH
 (IU/mice,ip) ACTH (mg/kg,ip)

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