CHAPTER IV

RESULTS

Chemical identification of the dried-stem paste of *C. quadrangularis*

Chromatographic fingerprint of the crude extract of *C. quadrangularis* dried stems (CQ) used in this study (Figure 4-1) conformed with somewhat difference to the chromatographic fingerprint of the reference petroleum ether extract of *C. quadrangularis* reported earlier (Figure 4-2, ธัญวรัตน์ จันทรชนะ และ พงศธร หลิมศิริวงษ์, 2543). Likewise, the extract exhibited a positive result to the anisaldehyde-sulfuric acid color test (Figure 4-3). These characteristics of the crude extract of *C. quadrangularis* dried stems were indicated to be composed of triterpenes and phytosterol (Pluemjai et al., 1986).

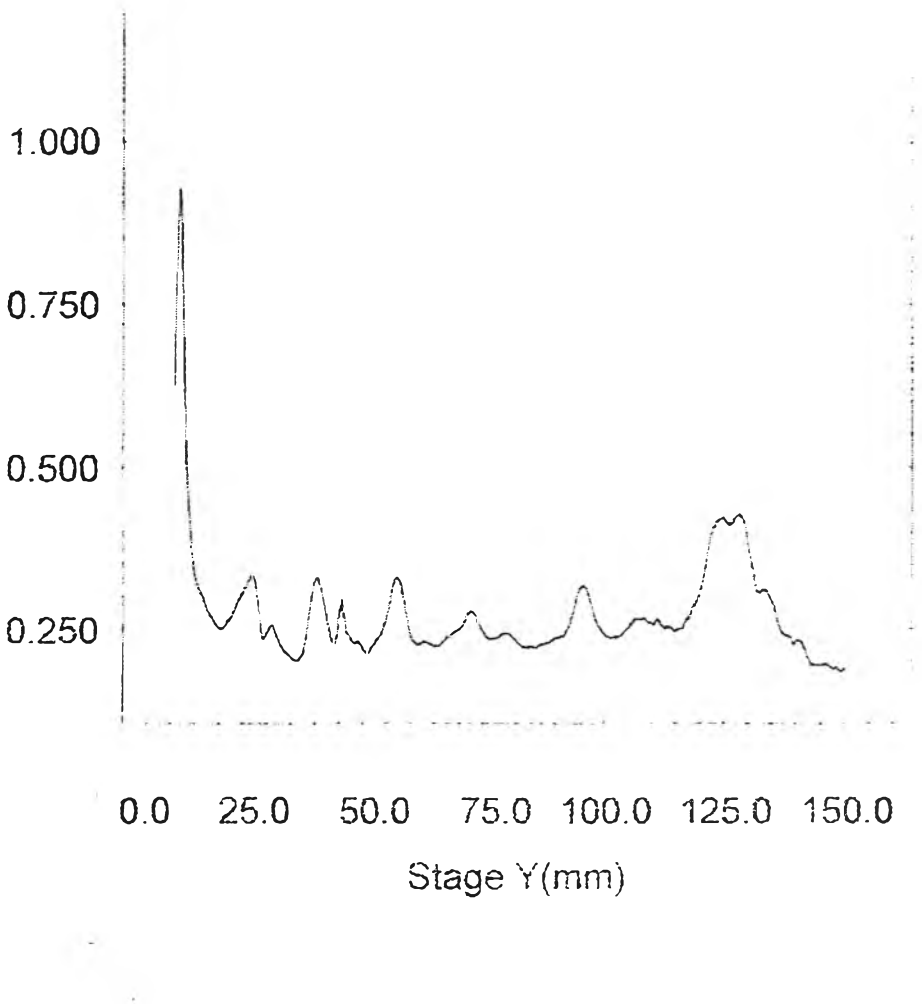

Figure 4-1 The chromatographic fingerprint of the crude extract of *C. quadrangularis* dried stems used in this study

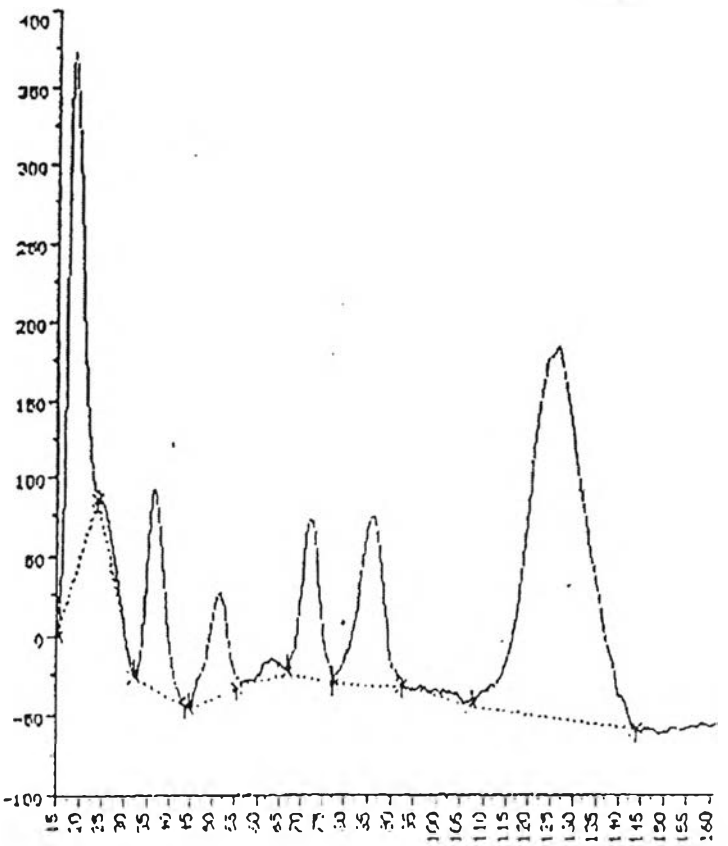

Figure 4-2 The chromatographic fingerprint of the the dried-stem powder of *C. quadrangularis* used as reference (ธัญวรัตน์ จันทรชนะ และ พงศธร หลิมศิริวงษ์, 2543)

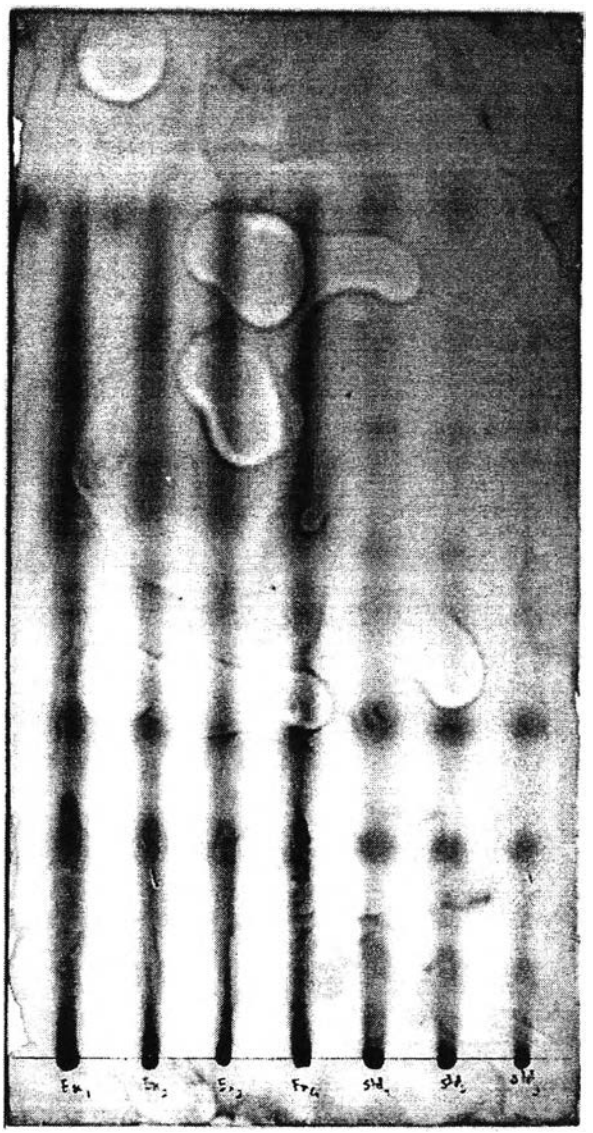

Figure 4-3 The TLC plate of the crude extract of *C. quadrangularis* dried stem. Following the densitometric determination, the TLC plate was sprayed with the mixture solution of anisaldehyde-sulfuric acid, heated at 105 °C for 5 min (Procedure was mentioned in Materials and Methods). All lanes were spotted with the crude extract of *C. quadrangularis* dried stems used in this study.

MOUSE HOT-PLATE TEST

To demonstrate the validity of the hot-plate analgesic testing following intraperitoneal (i.p.) drug administration, mice received morphine sulphate (MO; 10 mg/kg) i.p. and were tested during the subsequent 240 min period. As expected MO significantly ($p<0.01$) increased hot-plate latency producing an area of analgesia of 8,043.82±3,609.21 %MPE-min compared with that of normal saline solution (NSS) (-1,914.82±4499.06 %MPE-min; Figure 4-4). The i.p. administration of acetylsalicylic acid (ASA; 150 mg/kg), a nonsteroidal anti-inflammatory drug (NSAIDs), also influenced the hot-plate latency and area of analgesia when compared to NSS ($p<0.01$; Figure 4-5)

Initial studies utilizing the hot-plate test in mice to examine the efficacy of the crude extract of *Cissus quadrangularis* dried stems (CQ) in producing analgesia. Mice were then administered NSS or various doses of CQ (43.5, 87.5, 175, 350, and 700 mg/kg) i.p. CQ doses of 43.5 mg/kg or higher produced significant ($p<0.05$, $p<0.05$, $p<0.01$, $p<0.01$, $p<0.01$, respectively) analgesic responses compared to NSS (Figure 4-6). MO showed the highest analgesic response compared to all test groups. CQ dose 175 mg/kg produced analgesic response similar to ASA (Figure 4-7).

When the log of the CQ dose was plotted versus the area of analgesia, a significant linear correlation was observed. When all five doses of CQ (43.5, 87.5, 175, 350, and 700 mg/kg) were plotted a significant linear correlation coefficient (r^2) equal to 0.82 was observed, while the plotting of only four doses (43.5, 87.5, 175, and 350 mg/kg) revealed a significant linear correlation coefficient of 0.97 (Figure 4-8 & 4-9). ED_{50} was calculated from the log dose probit line and was equal to 440.62 (44.28 - 4384.77) mg/kg (Figure 4-10).The analgesic peak effect of CQ was reached within 90 min after i.p. administration in all CQ doses tested and individual time courses of the responses are shown in Figure 4-11.

In order to investigate any role of the opioid receptor in CQ actions, mice were then administered i.p. NSS, naloxone (NAL; 1 mg/kg), an opioid receptor antagonist, CQ (175, 350, 700 mg/kg) or the combination of naloxone and CQ (1/175, 1/350, and 1/700 mg/kg). Naloxone alone failed to produce significant responses when compared to vehicle control. CQ (175, 350, and 700 mg/kg) produced significant ($p<0.01$, $p<0.01$, $p<0.01$, respectively) responses when compared to vehicle control. The inclusion of naloxone with all dose of CQ did not produce significant responses when compared to CQ alone (Figure 4-12 to 4-15). Additionally, naltrexone (NALT; 5 mg/kg), an opioid receptor antagonist, CQ (175, 350, 700 mg/kg) or the combination of naltrexone and CQ (5/175, 5/350, and 5/700 mg/kg) were administered i.p.. Naltrexone alone failed to produce significant responses when compared to vehicle control. CQ (175, 350, and 700 mg/kg) produced significant ($p<0.05$, $p<0.01$, $p<0.01$, respectively) responses when compared to vehicle control. CQ (175, 350, and 700 mg/kg) produced significant ($p<0.05$, $p<0.01$, $p<0.01$, respectively) responses when compared to NALT. The inclusion of naltrexone with CQ doses of 350 and 700 mg/kg significantly ($p<0.05$, $p<0.05$, respectively) attenuated the analgesic response due to CQ (350 and 700 mg/kg) indicating that opioid receptors are most likely involved in the analgesic response produced by CQ (Figure 4-16 to 4-19).

To further explore the mechanism of CQ in this analgesic testing model, mice were then administered i.p. NSS, N-methyl-D-aspartic acid (NMDA; 0.38 mg/kg), CQ (175, 350, and 700 mg/kg) or the combination or NMDA and CQ (0.38/175, 0.38/350, and 0.38/700 mg/kg). NMDA alone failed to produce significant analgesic responses when compared to vehicle control. CQ (175, 350, and 700 mg/kg) produced significant ($p<0.05$, $p<0.01$, $p<0.05$, respectively) analgesic responses when compared to vehicle control. The inclusion of NMDA did not produce significant responses when compared to CQ alone (Figure 4-20 to 4-23).

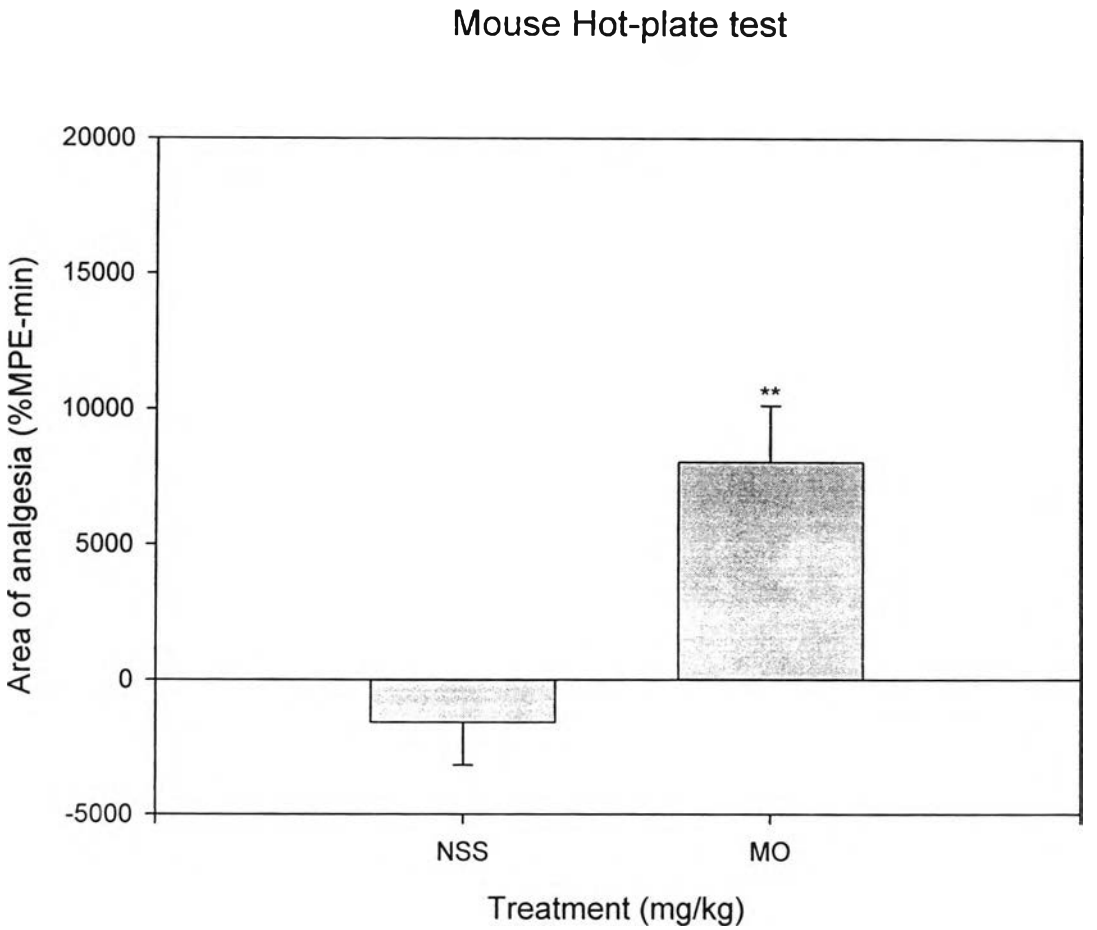

Figure 4-4 Area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS) and morphine sulphate (MO; 10 mg/kg) N=10 for all groups. ** $p < 0.01$ significantly different compared to NSS.

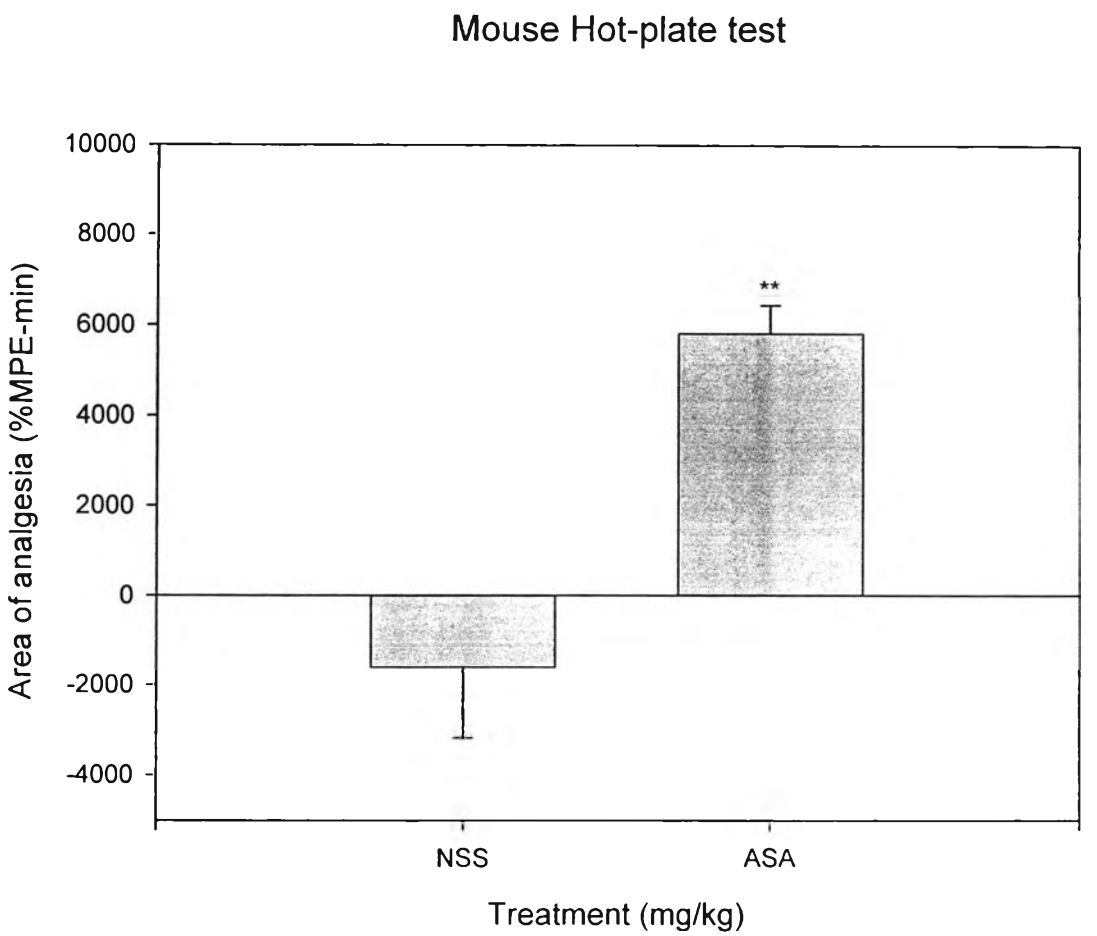

Figure 4-5 Area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS) and acetylsalicylic acid (ASA; 150 mg/kg) N=10 for all groups. ** $p < 0.01$ significantly different compared to NSS.

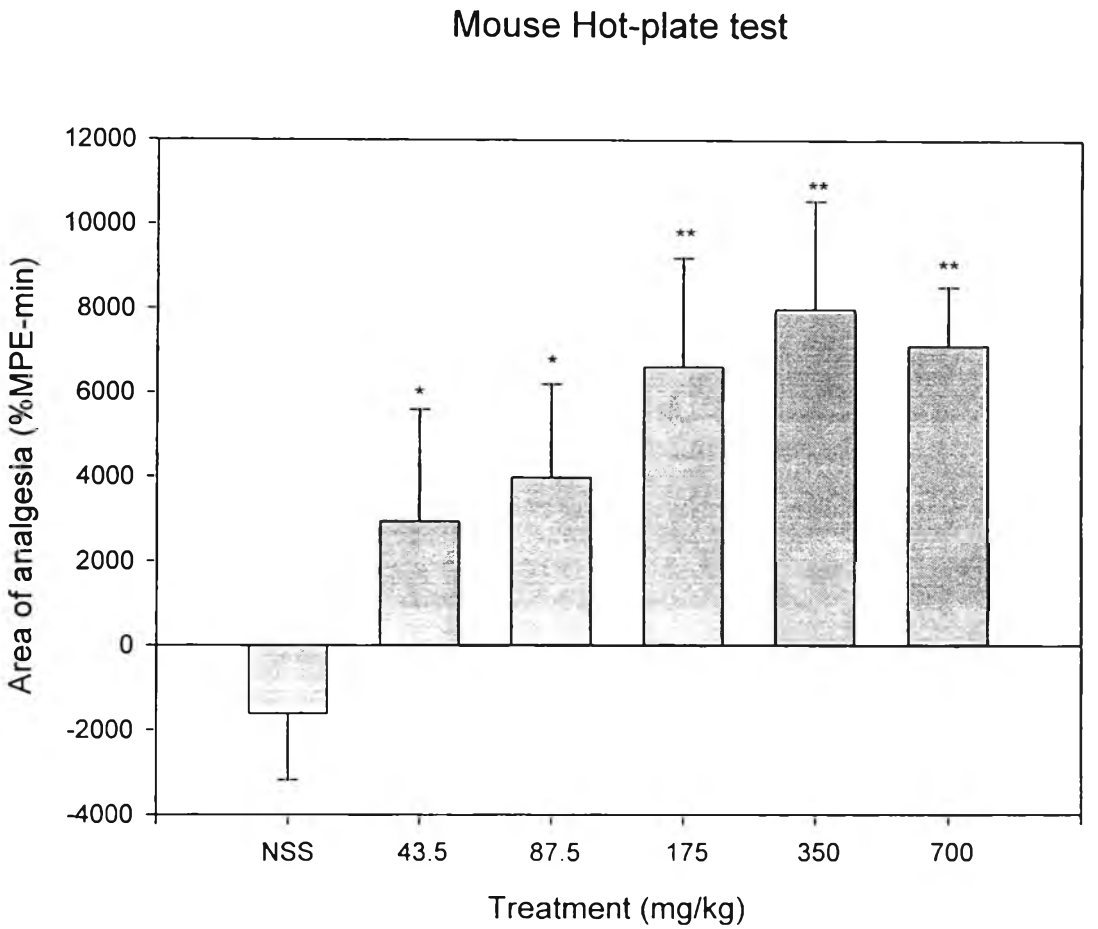

Figure 4-6 Area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS) and the crude extract of *C. quadrangularis* dried stems (CQ; 43.5-700 mg/kg). N=10 for all groups. * $p < 0.05$,** $p < 0.01$ significantly different compared to NSS.

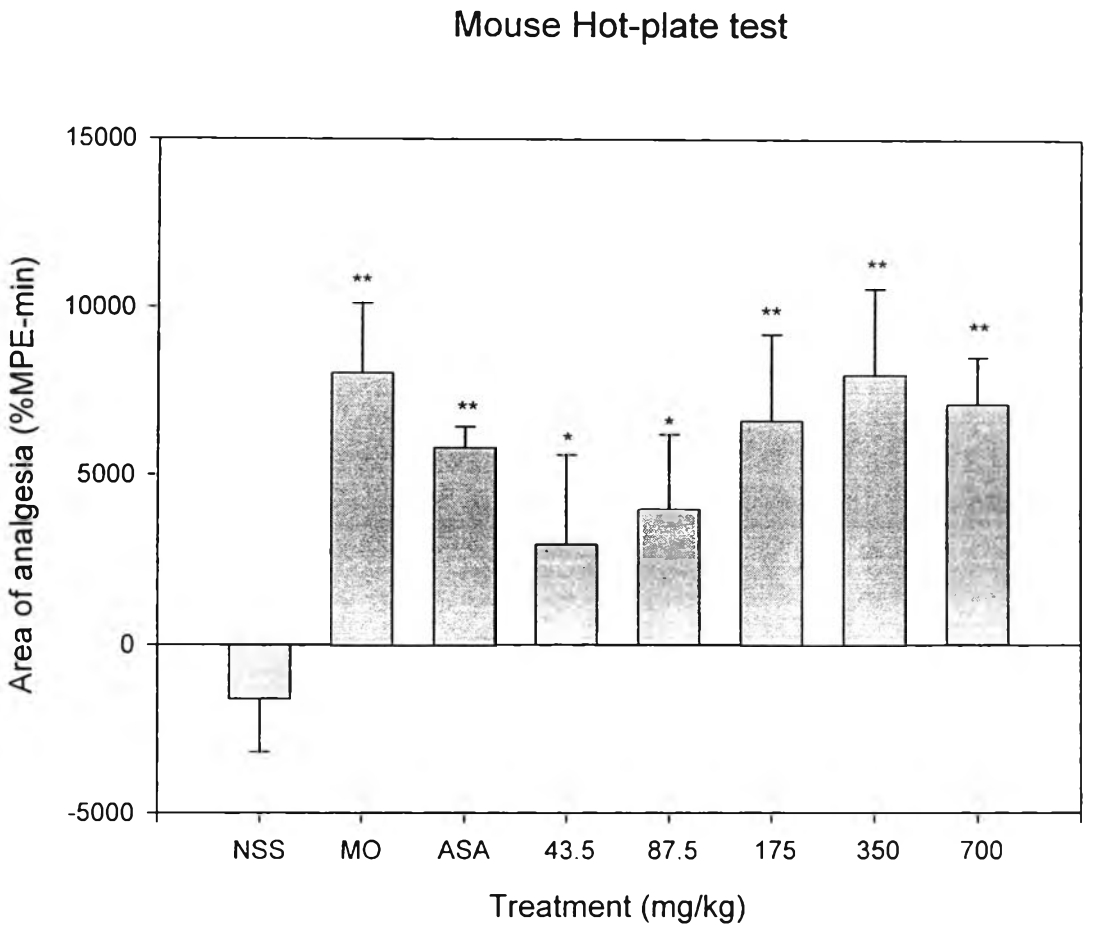

Figure 4-7 Area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS), MO (10 mg/kg), ASA (150 mg/kg) and various doses of CQ (43.5-700 mg/kg). N=10 for all groups. * $p < 0.05$,** $p < 0.01$ significantly different compared to NSS.

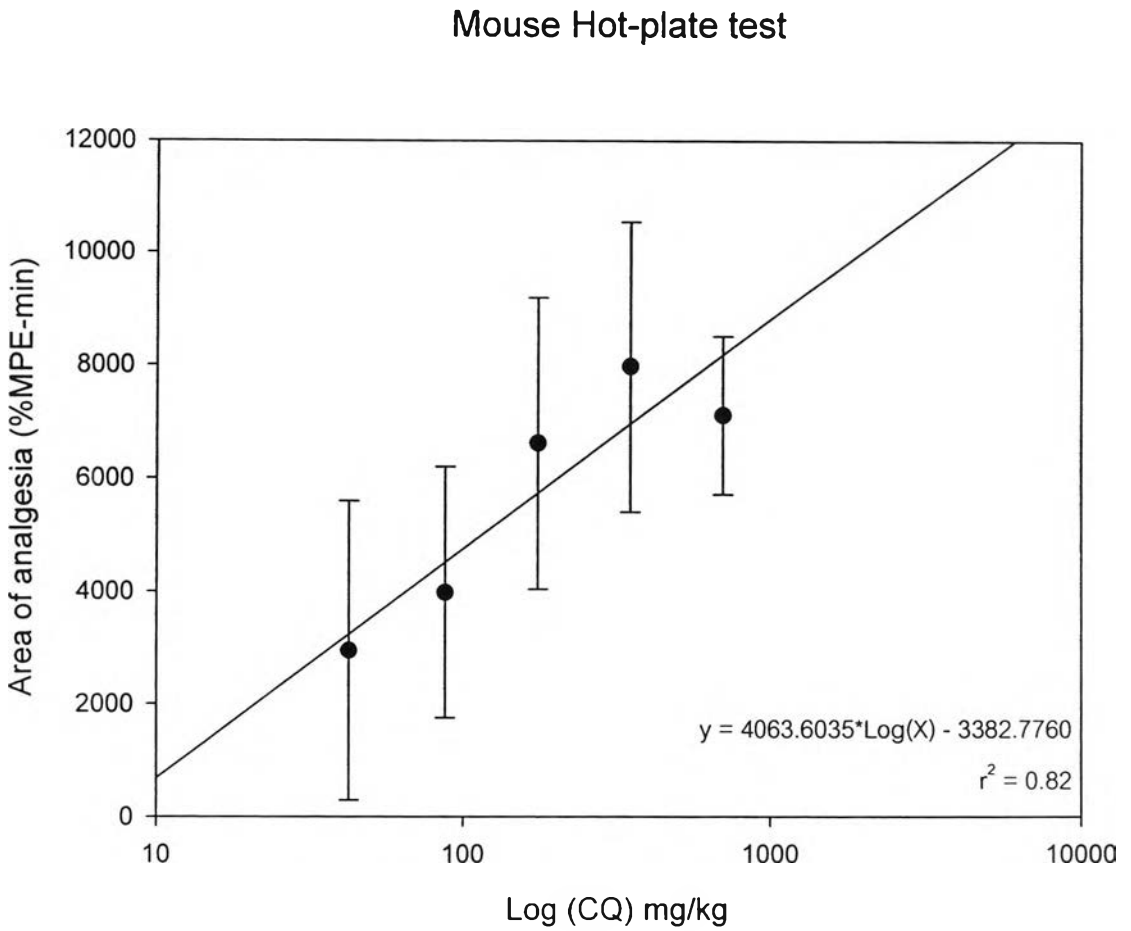

Figure 4-8 Linear regression of area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of the crude extract of *C. quadrangularis* dried stems (CQ; 43.5-700 mg/kg). N=10 for all groups. The regression equation was Y = 4063.6035*LOG(X) - 3382.7760 , r^2 = 0.82

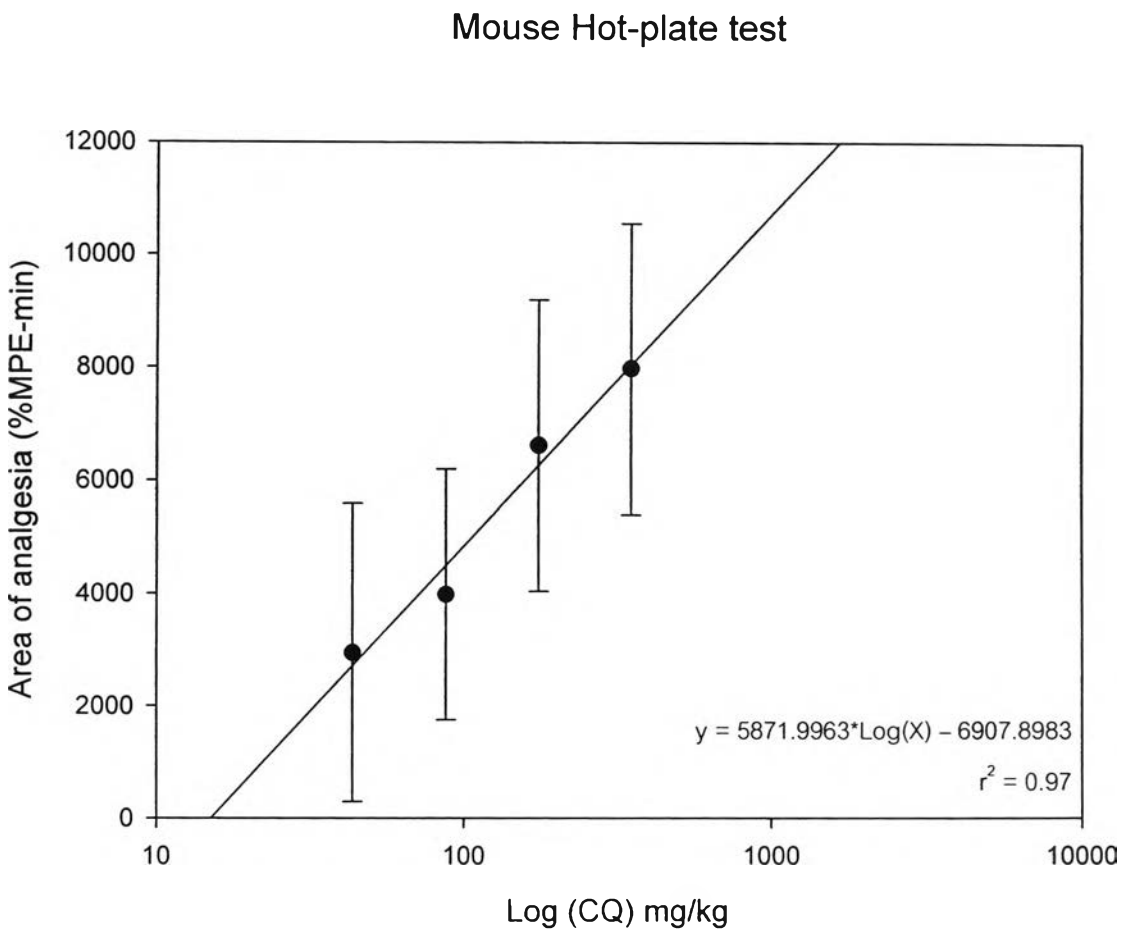

Figure 4-9 Linear regression of area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of the crude extract of *C. quadrangularis* dried stems (CQ; 43.5-350 mg/kg). N=10 for all groups. The regression equation was Y = 5871.9963*LOG(X) - 6907.8983, r^2 = 0.97

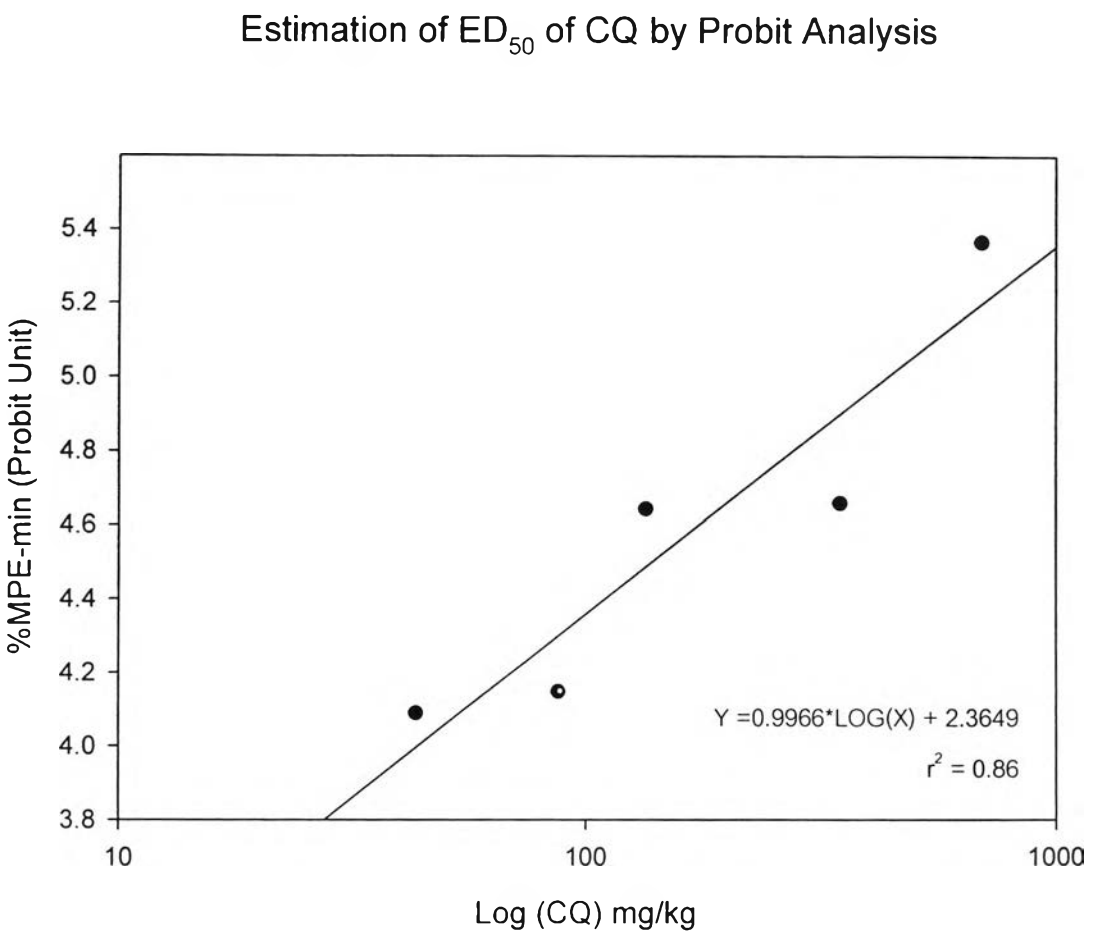

Figure 4-10 Linear regression of %MPE (Probit unit) at 90 minutes after intraperitoneal administration of various doses of CQ (43.5-700 mg/kg) using hot-plate test. N=10 for all groups. The ED_{50} was calculated from the log dose probit line as Y =0.9966*LOG(X) + 2.3649, r^2 = 0.86 and equal to $_{440.61}$ ($_{44.28 - 4384.77}$) mg/kg

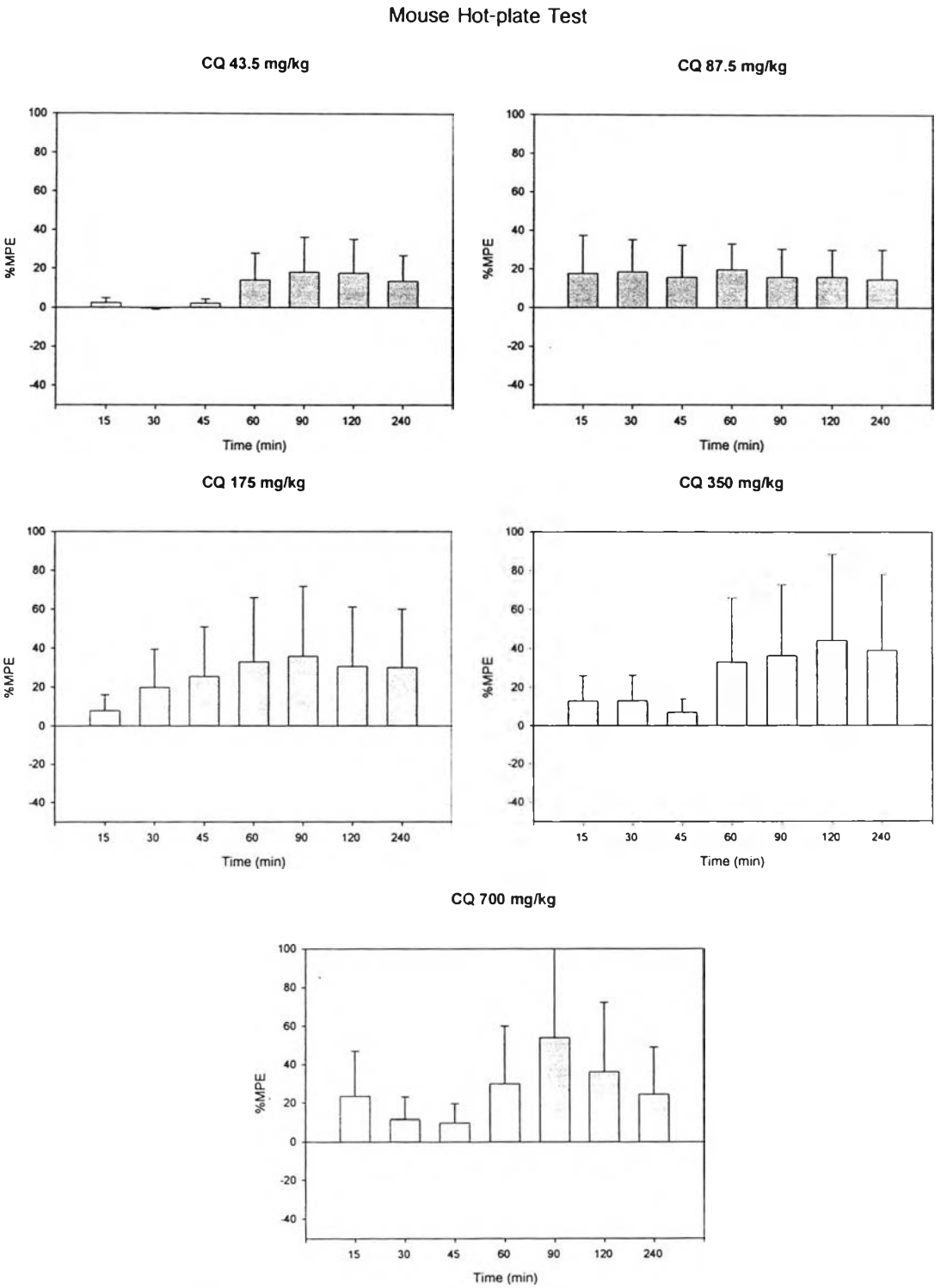

Figure 4-11 Individual time courses of the response (%MPE versus time (min)) after intraperitoneal administration of various doses of CQ (43.5-700 mg/kg). N=10 for all groups.

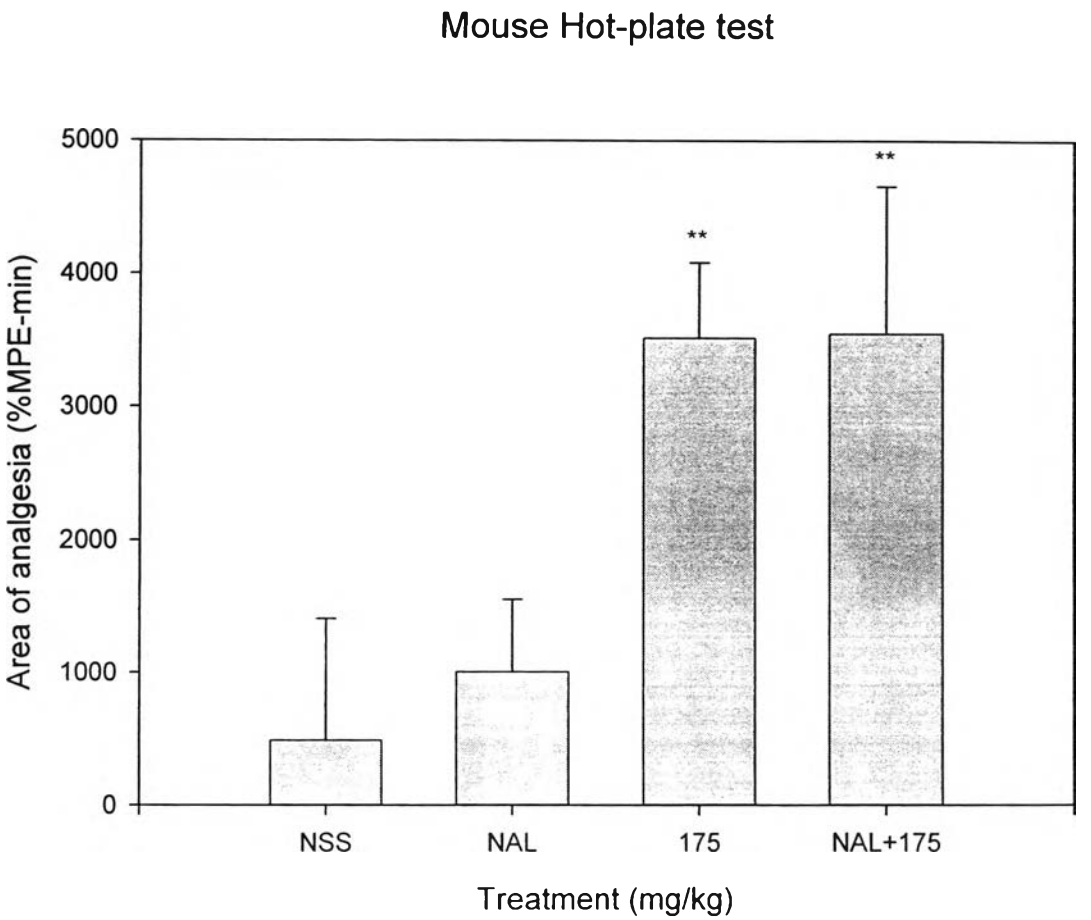

Figure 4-12 Area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS), CQ (175 mg/kg), Naloxone (NAL; 1 mg/kg), and NAL + CQ (1/175 mg/kg). N=10 for all groups. ** $p < 0.01$ significantly different compared to NSS.

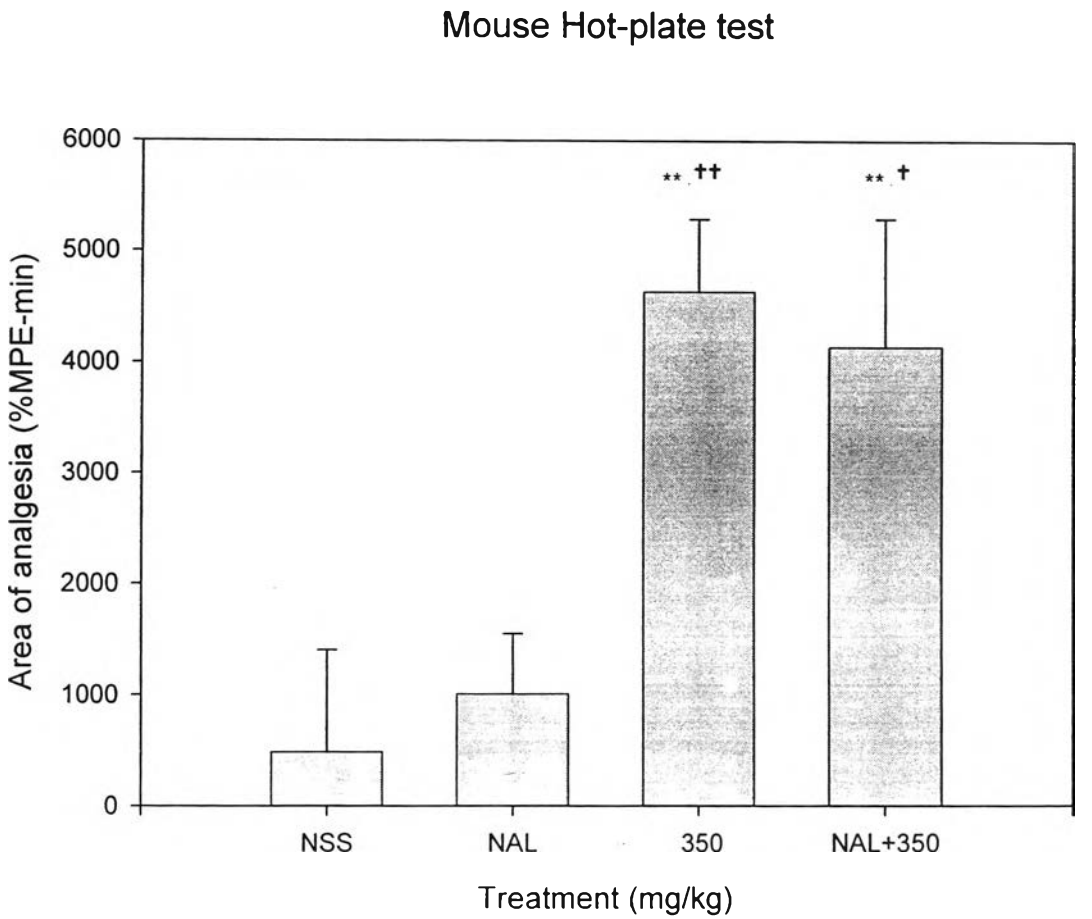

Figure 4-13 Area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS), CQ (350 mg/kg), Naloxone (NAL; 1 mg/kg), and NAL + CQ (1/350 mg/kg). N=10 for all groups. ** $p < 0.01$ significantly different compared to NSS. † $p < 0.05$, †† $p < 0.01$ significantly different compared to NAL.

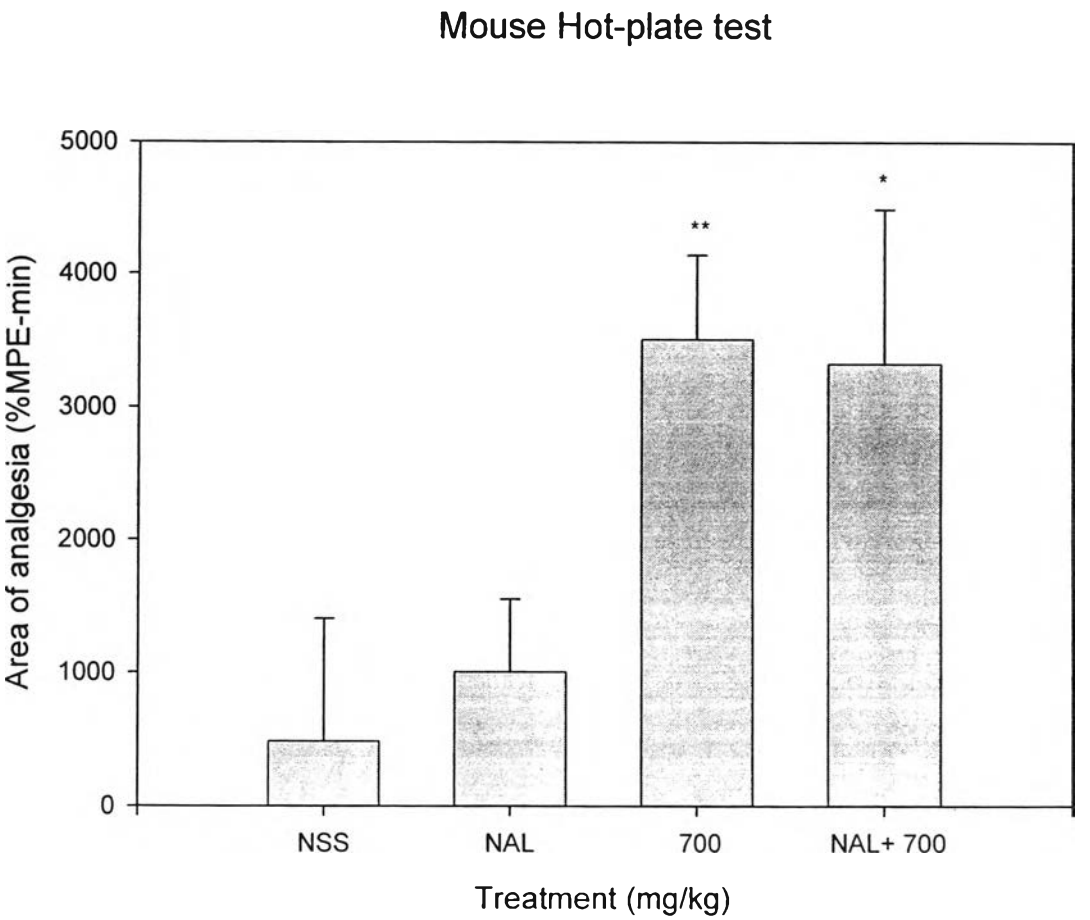

Figure 4-14 Area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS), CQ (700 mg/kg), Naloxone (NAL; 1 mg/kg), and NAL + CQ (1/700 mg/kg). N=10 for all groups. * $p < 0.05$,** $p < 0.01$ significantly different compared to NSS.

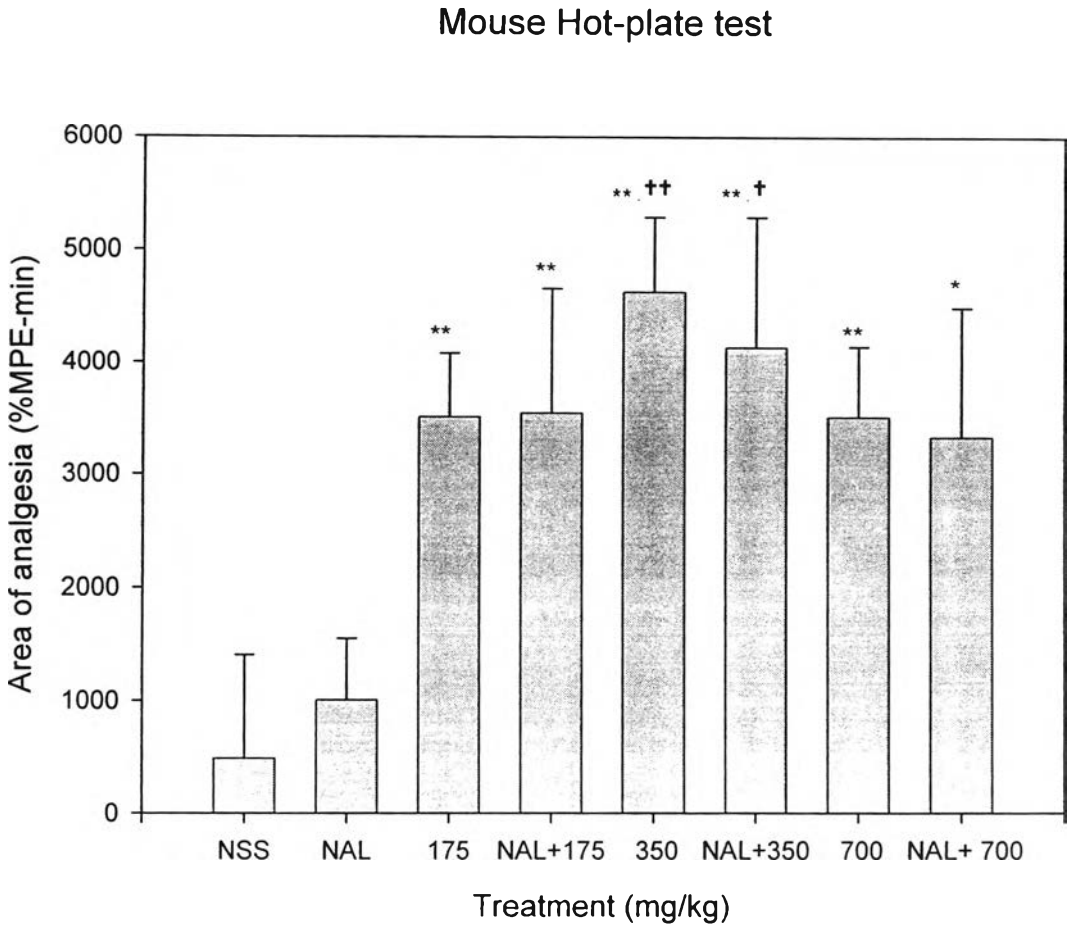

Figure 4-15 Area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS), CQ (175, 350 and 700 mg/kg), Naloxone (NAL; 1 mg/kg), and NAL + CQ (1/175, 1/350, 1/700 mg/kg). N=10 for all groups. * $p < 0.05$,** $p < 0.01$ significantly different compared to NSS. † $p< 0.05$, †† $p< 0.01$ significantly different compared to NAL.

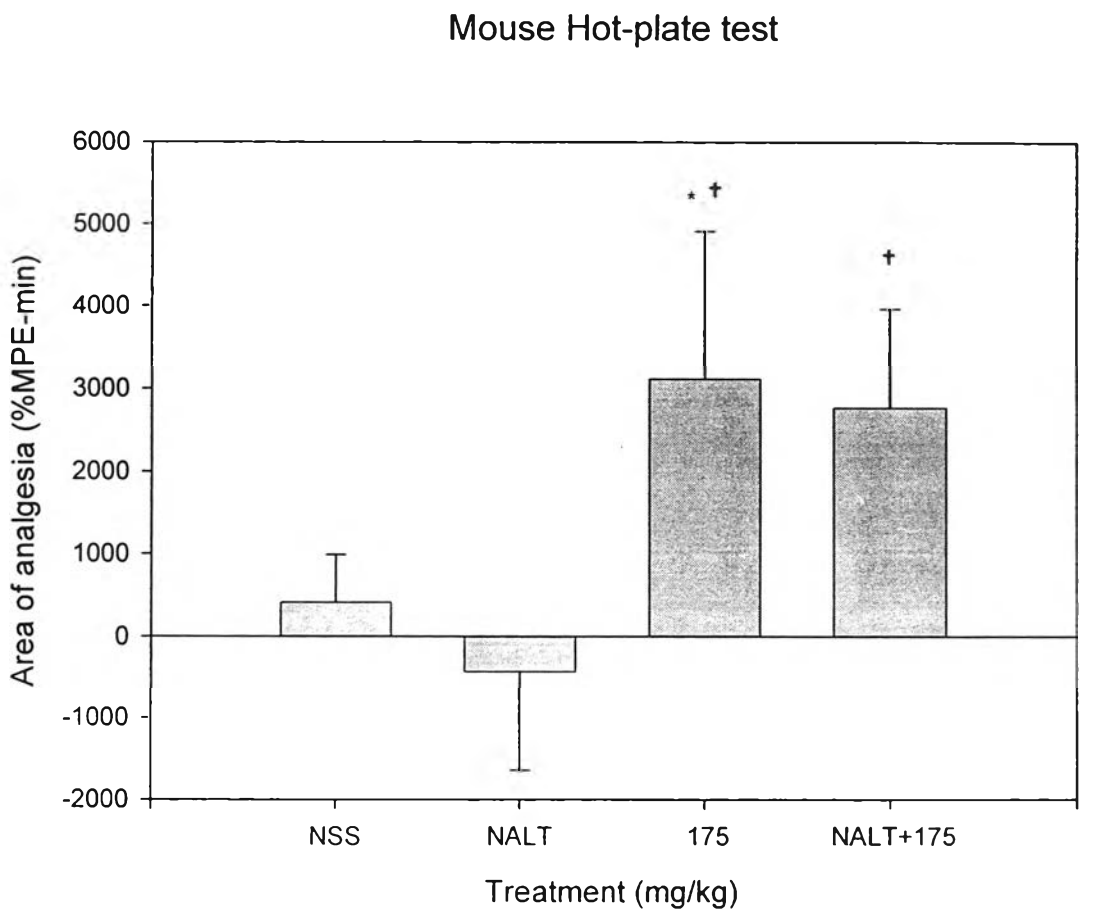

Figure 4-16 Area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS), CQ (175 mg/kg), Naltrxone (NALT; 5 mg/kg), and NALT + CQ (5/175 mg/kg). N=10 for all groups. * $p< 0.05$ † $p< 0.05$ significantly different compared to NALT.

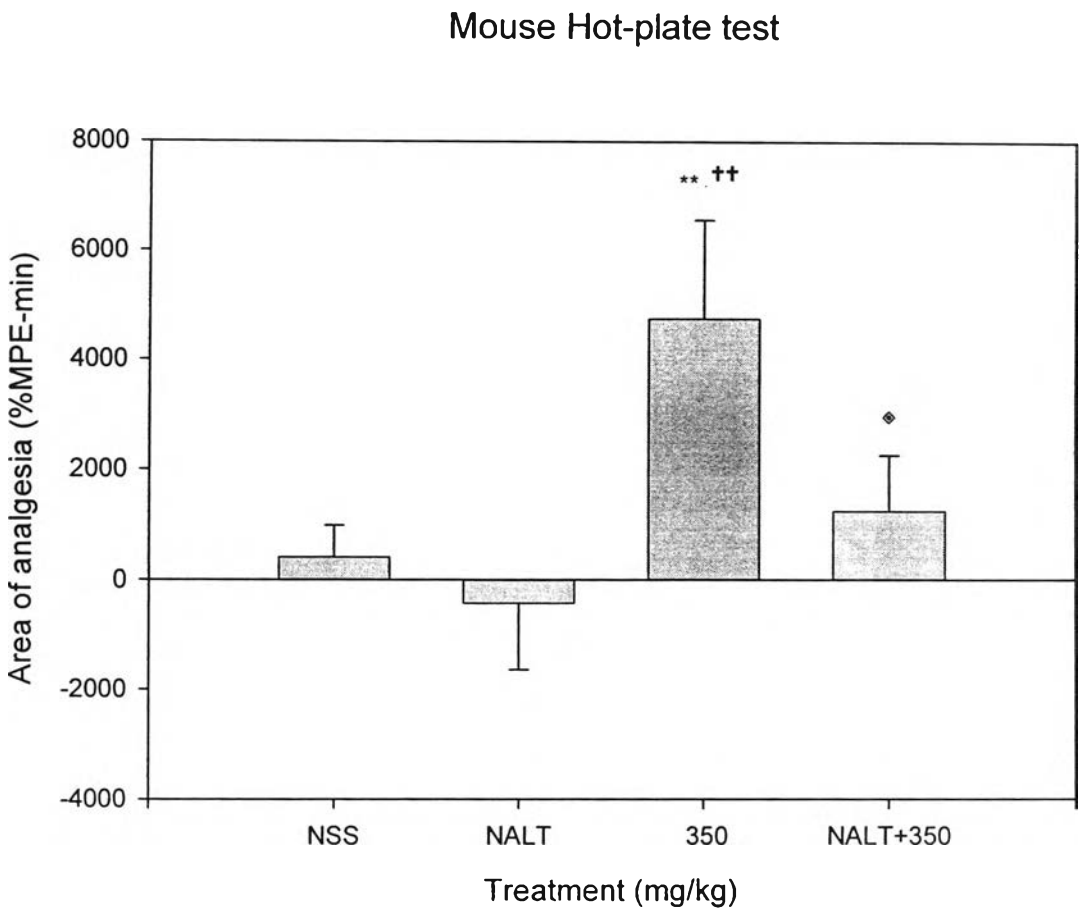

Figure 4-17 Area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS), CQ (350 mg/kg), Naltrxone (NALT; 5 mg/kg), and NALT + CQ (5/350 mg/kg). N=10 for all groups. ** $p< 0.01$ significantly different compared to NSS. †† $p< 0.01$ significantly different compared to NALT. ◈ $p< 0.05$ significantly different compared to CQ 350.

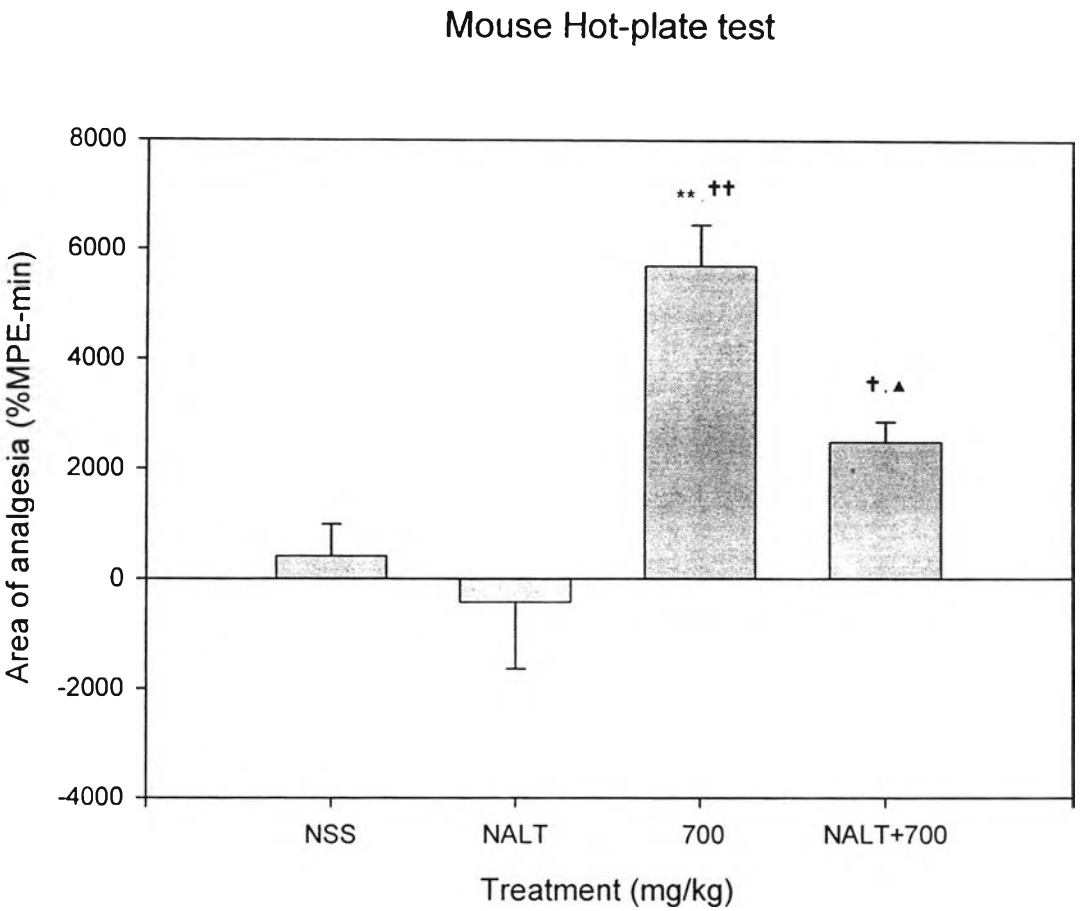

Figure 4-18 Area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS), CQ (700 mglkg), Naltrxone (NALT; 5 mg/kg), and NALT + CQ (5/700 mg/kg). N=10 for all groups. ** $p< 0.01$ significantly different compared to NSS. †† $p< 0.01$ significantly different compared to NALT. ▲ $p < 0.05$ significantly different compared to CQ 700.

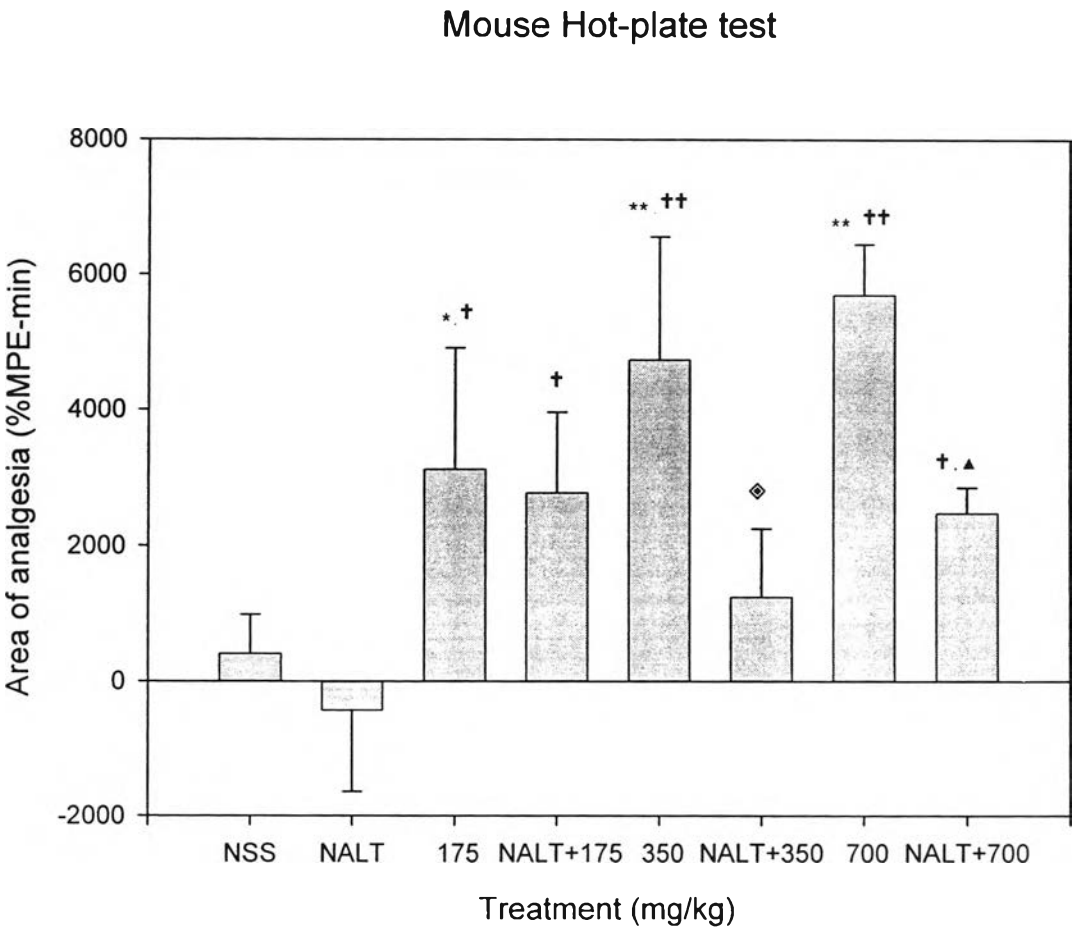

Figure 4-19 Area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS), CQ (175, 350 and 700 mglkg), Naltrxone (NALT; 5 mg/kg), and NALT + CQ (5/175, 5/350, 5/700 mg/kg). N=10 for all groups. * $p< 0.05$,** $p< 0.01$ significantly different compared to NSS. † $p< 0.05$,†† $p< 0.01$ significantly different compared to NALT. ◈ $p< 0.05$ significantly different compared to CQ 350. ▲ $p < 0.05$ significantly different compared to CQ 700.

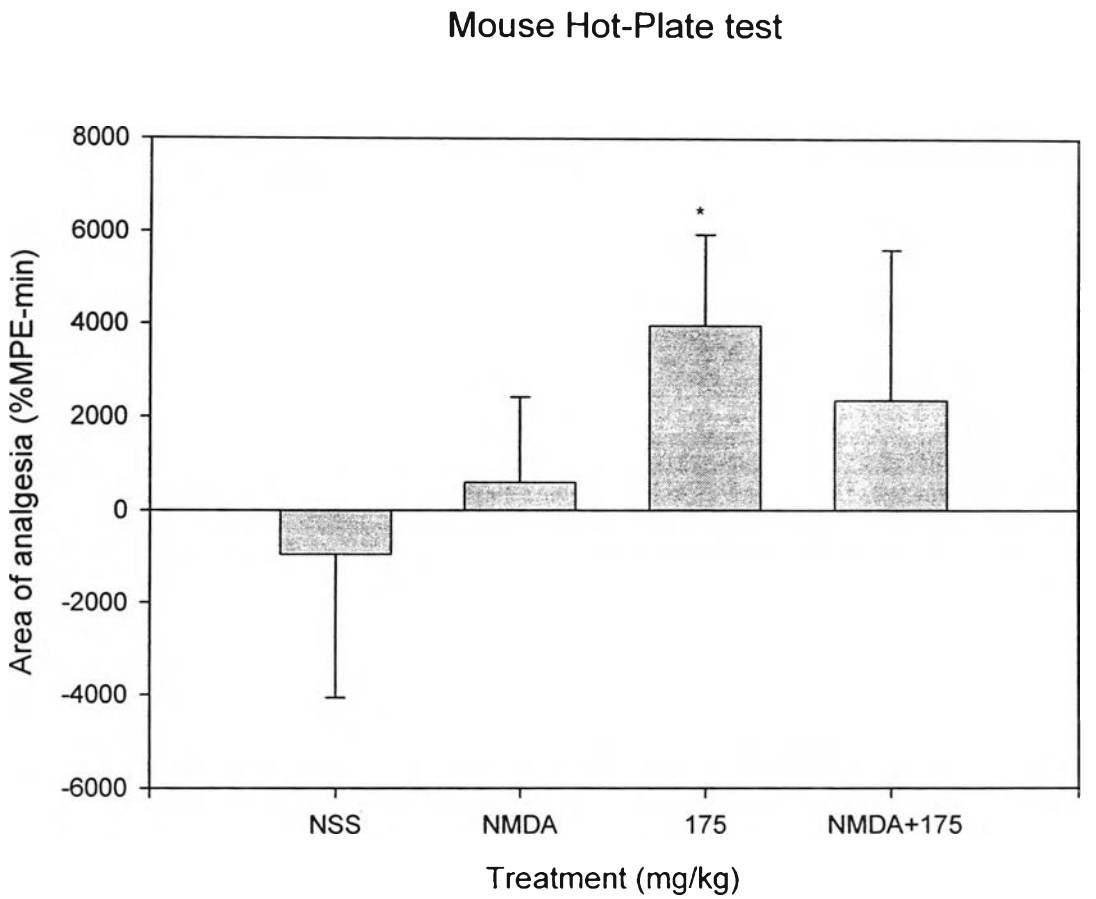

Figure 4-20 Area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS), CQ (175 mg/kg), NMDA (0.38 mg/kg), and NMDA + CQ (0.38/175 mg/kg). N=10 for all groups. * $p < 0.05$ significantly different compared to NSS.

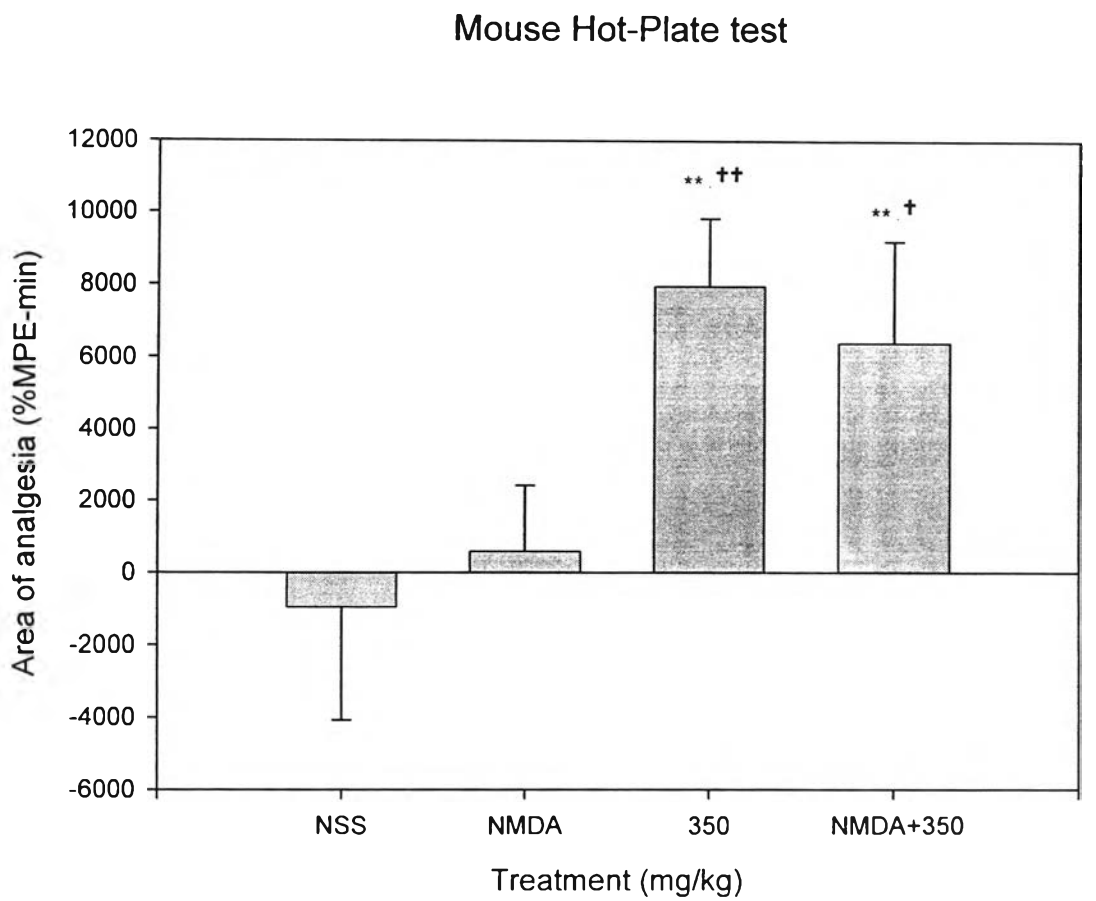

Figure 4-21 Area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS), CQ (350 mg/kg), NMDA (0.38 mg/kg), and NMDA + CQ (0.38/350 mg/kg). N=10 for all groups. ** $p < 0.01$ significantly different compared to NSS. † $p< 0.05$, †† $p< 0.01$ significantly different compared to NMDA

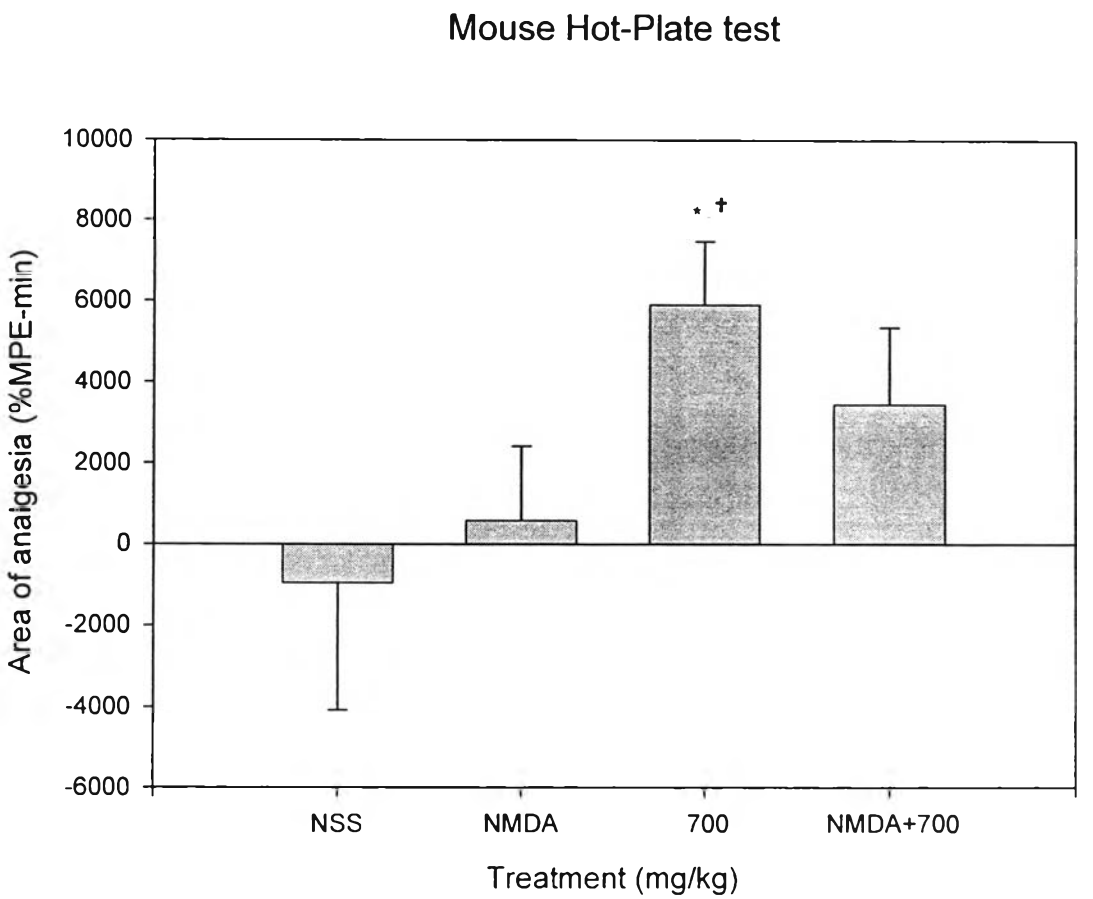

Figure 4-22 Area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS), CQ (700 mg/kg), NMDA (0.38 mg/kg), and NMDA + CQ (0.38/700 mg/kg). N=10 for all groups. * $p < 0.05$ significantly different compared to NSS. † $p < 0.05$ significantly different compared to NMDA

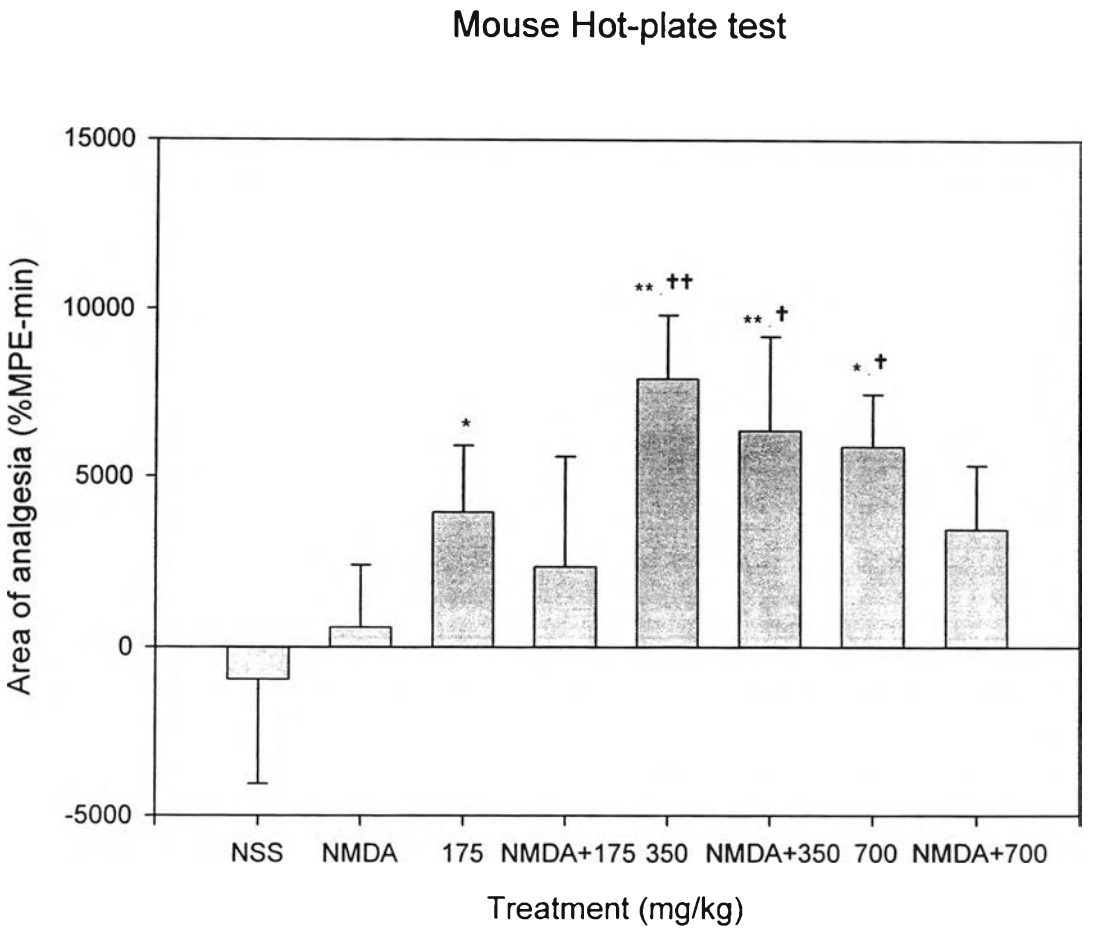

Figure 4-23 Area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS), CQ (175, 350 and 700 mg/kg), NMDA (0.38 mg/kg), and NMDA + CQ (0.38/175, 0.38/350, 0.38/700 mg/kg). N=10 for all groups. * $p < 0.05$,** $p < 0.01$ significantly different compared to NSS. † $p < 0.05$,†† $p < 0.01$ significantly different compared to NMDA

MOUSE TAIL-FLICK TEST

To demonstrate the validity of the mouse tail-flick analgesic testing following i.p. drug administration, mice received morphine sulphate (MO; 10 mg/kg) i.p. and were tested during the subsequent 240 min period. As expected MO significantly *($p<0.01$)* increased tail-flick latency producing an area of analgesia of 9966.92±516.46 %MPE-min compared with that of NSS (-362.41±694.93 %MPE-min; Figure 4-24). The i.p. administration of ASA (150 mg/kg) also influenced the tail-flick latency and area of analgesia when compared to NSS ($p<0.01$; Figure 4-25).

Studies then utilized the mouse tail-flick method to examine the efficacy of CQ in producing analgesia. Mice were injected i.p. NSS or various doses of CQ (43.5, 87.5, 175, 350, and 700 mg/kg). CQ doses of 87.5 mg/kg or higher significantly ($p<0.05$, $p<0.01$, $p<0.01$, $p<0.01$, respectively) increased tail-flick latency when compared to NSS. Additionally, CQ doses of 350 mg/kg and higher also significantly ($p<0.05$, $p<0.01$, respectively) increased tail-flick latency when compare to the lowest dose of CQ used (Figure 4-26). MO showed the highest analgesic response compared to all test groups. CQ dose 175 mg/kg produced analgesic response similar to ASA (Figure 4-27).

When the log dose of CQ was plotted versus the area of analgesia, a significant linear correlation was observed. All five doses of CQ (43.5, 87.5, 175, 350, 700 mg/kg) were plotted a significant linear correlation coefficient (r^2) equal to 0.91 was observed (Figure 4-28). The analgesic peak effect of CQ was reached within 90 min after i.p. administration in all CQ doses tested and individual time courses of the responses are shown in Figure 4-29.

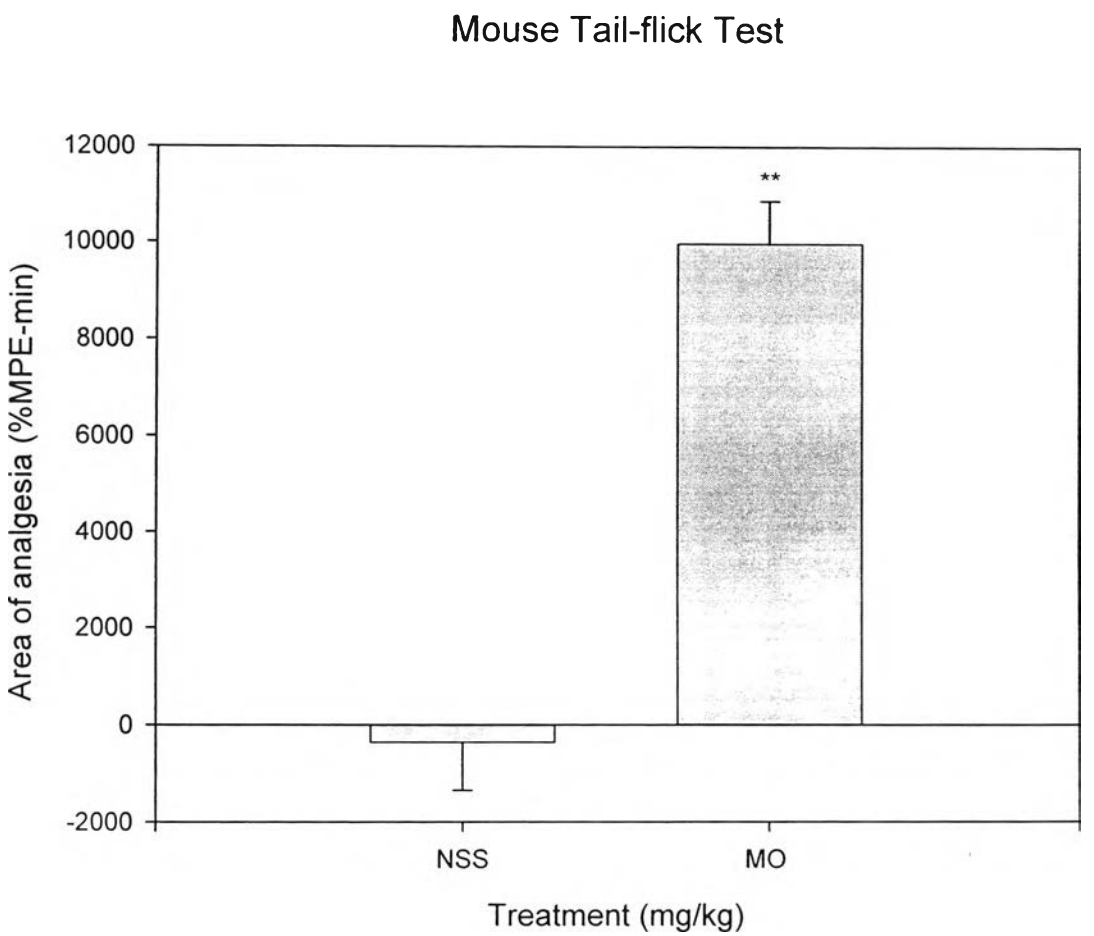

Figure 4-24 Area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS) and morphine sulphate (MO; 10 mg/kg). N=10 for all groups. ** $p < 0.01$ significantly different compared to NSS.

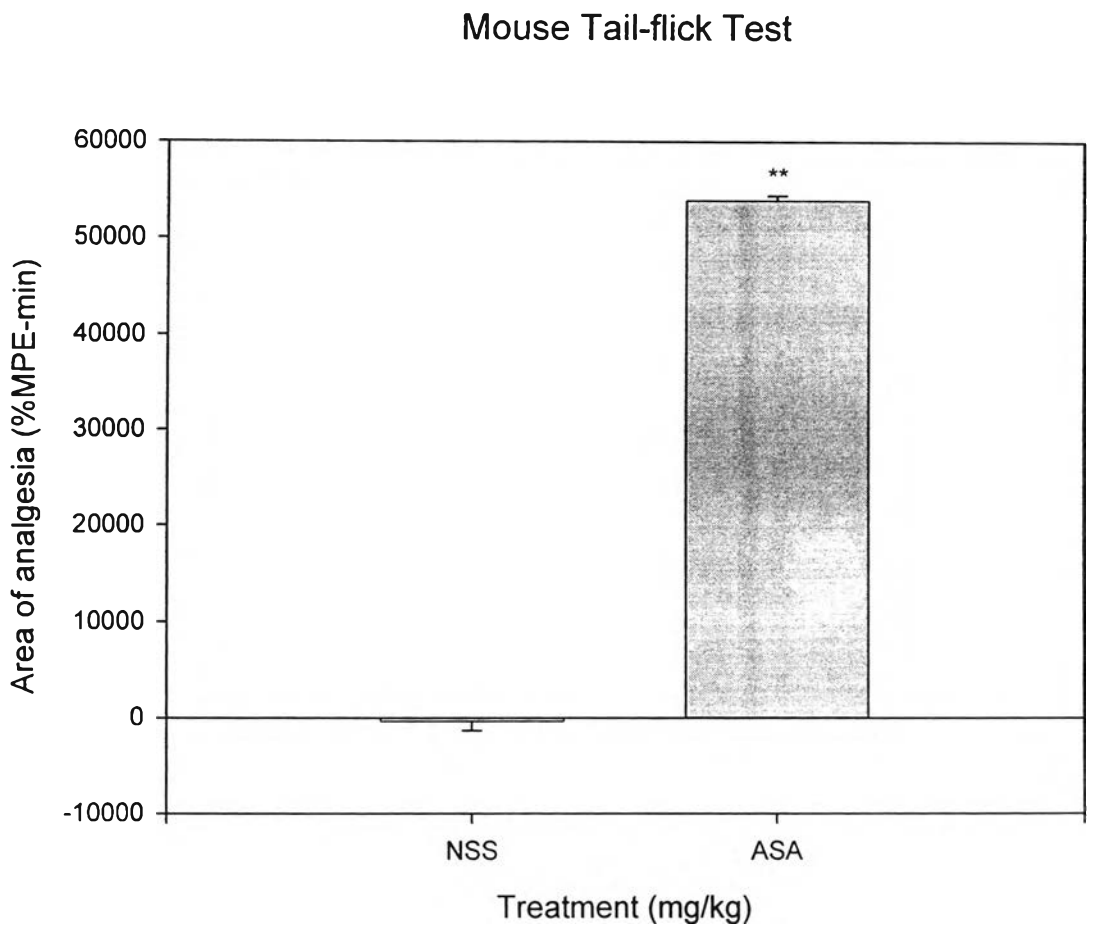

Figure 4-25 Area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS) and acetylsalicylic acid (ASA; 150 mg/kg) N=10 for all groups. ** $p < 0.01$ significantly different compared to NSS.

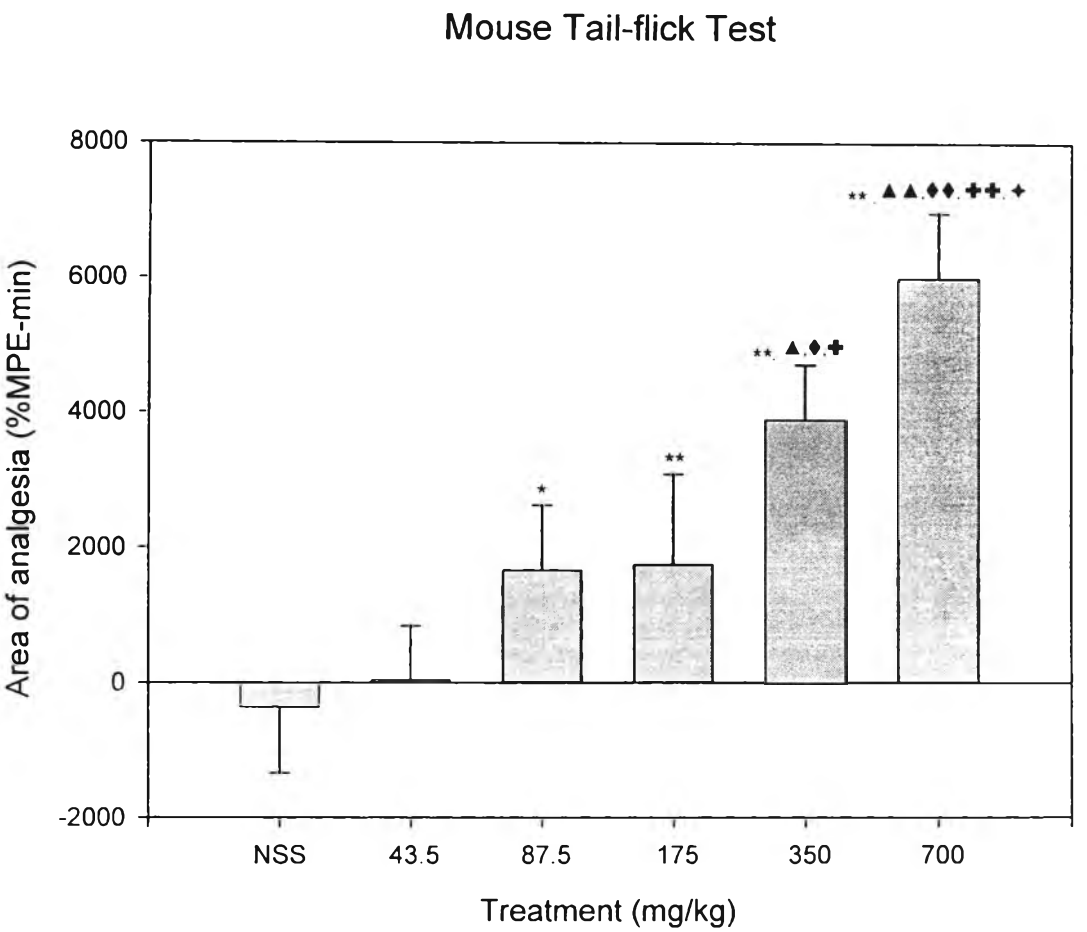

Figure 4-26 Area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS) and the crude extract of *C. quadrangularis* dried stems (CQ; 43.5-700 mg/kg). N=10 for all groups. * $p < 0.05$,** $p < 0.01$ significantly different compared to NSS. ▲ $p < 0.05$, ▲▲ $p < 0.01$ significantly different compared to CQ 43.5. ♦ $p < 0.05$, ♦♦ $p < 0.01$ significantly different compared to CQ 87.5. ✚ $p < 0.05$, ✚✚ $p < 0.01$ significantly different compared to CQ 175. ✦ $p < 0.05$ significantly different compared to CQ 350.

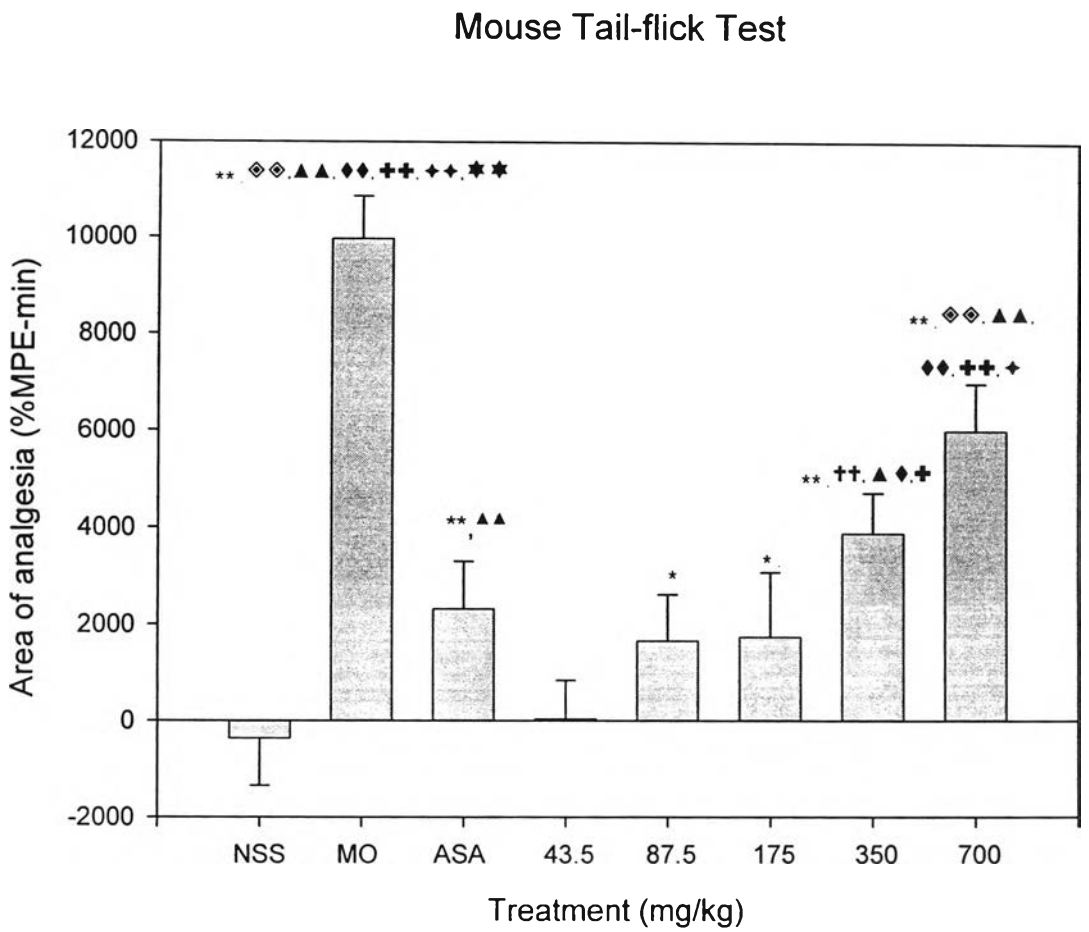

Figure 4-27 Area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS), MO (10 mg/kg), ASA (150 mg/kg) and various doses of CQ (43.5-700 mg/kg). N=10 for all groups. * $p< 0.05$, ** $p< 0.01$ significantly different compared to NSS. ◈◈ $p< 0.01$ significantly different compared to ASA. ▲ $p < 0.05$, ▲▲ $p < 0.01$ significantly different compared to CQ 43.5. ♦ $p < 0.05$, ♦♦ $p < 0.01$ significantly different compared to CQ 87.5. ✚ $p < 0.05$, ✚✚ $p < 0.01$ significantly different compared to CQ 175. ✦ $p < 0.05$, ✦✦ $p < 0.01$ significantly different compared to CQ 350. ✸✸ $p < 0.01$ significantly different compared to CQ 700.

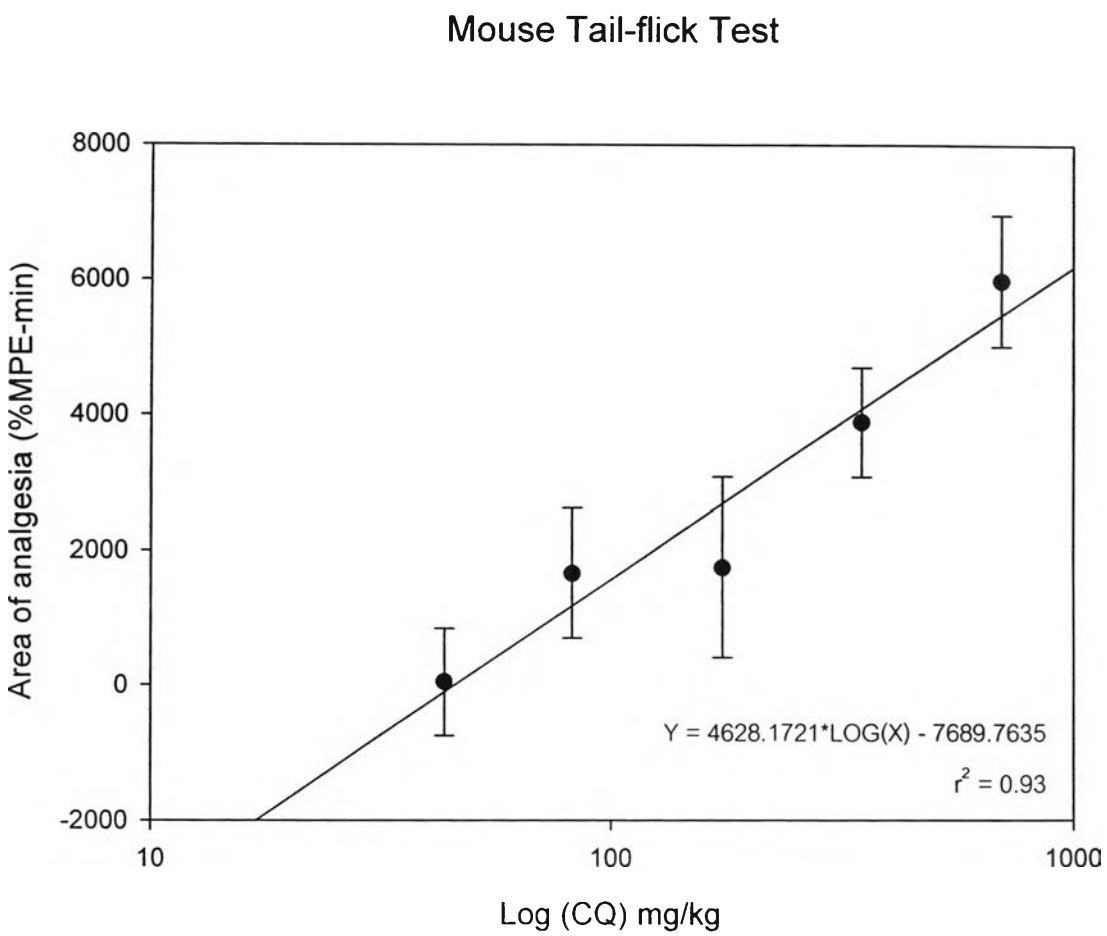

Figure 4-28 Linear regression of area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of the crude extract of *C. quadrangularis* dried stems (CQ; 43.5-700 mg/kg). N=10 for all groups. The regression equation was Y = 4628.1721*LOG(X) - 7689.7635, r^2 = 0.93

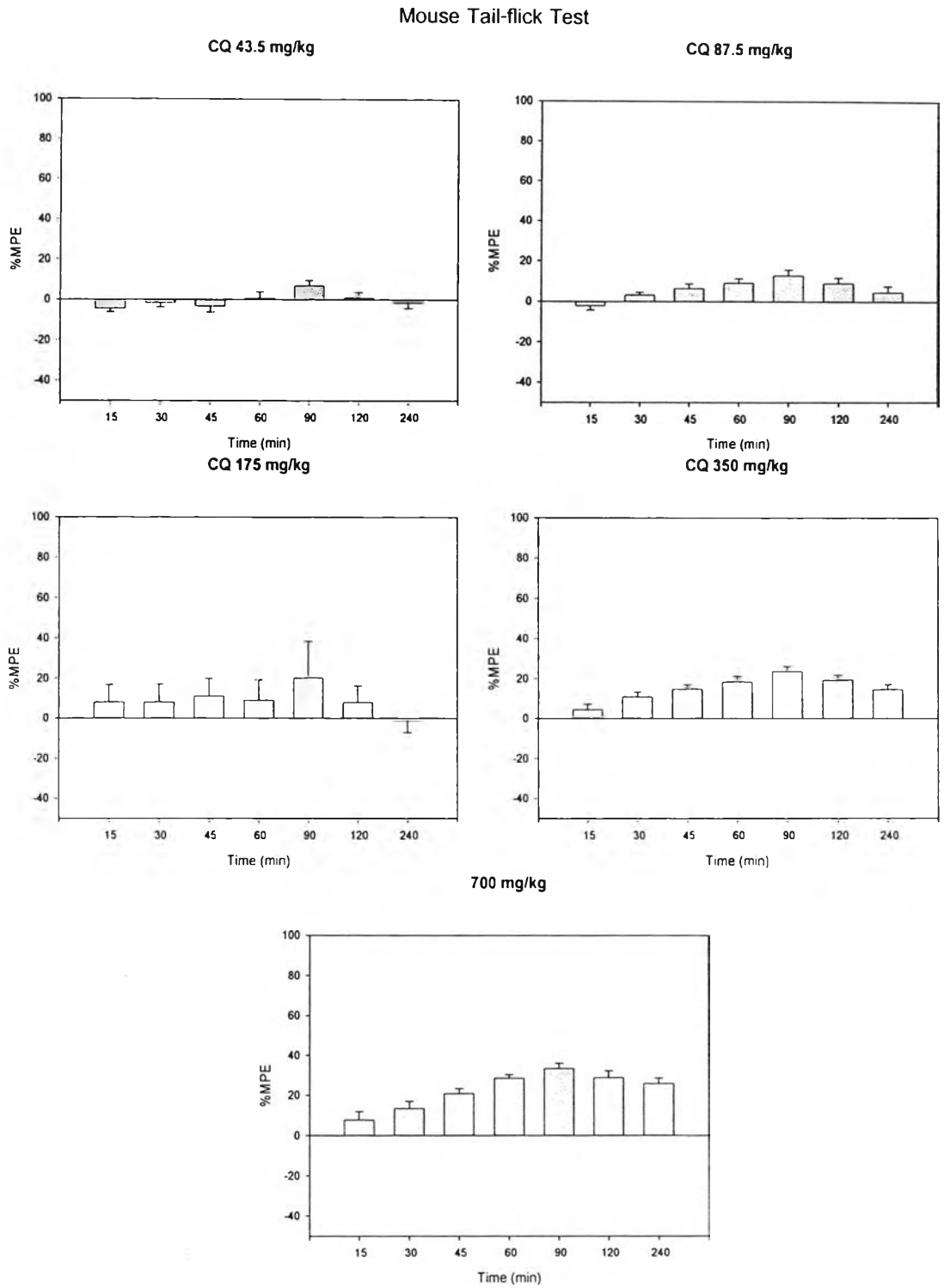

Figure 4-29 Individual time courses of the response (%MPE versus time (min)) after intraperitoneal administration of various doses of CQ (43.5-700 mg/kg). N=10 for all groups.

RAT PAW PRESSURE TEST

The studies were then conducted utilizing the Randall Selitto paw pressure technique. Initially, rats received i.p. NSS (1 ml/kg) or MO (10 mg/kg) and were tested during the subsequent 240 min period. MO significantly ($p<0.01$) increased the area of analgesia compared to vehicle group (Figure 4-30). The i.p. administration of ASA (150 mg/kg) also increased the pressure threshold and area of analgesia when compared to NSS ($p<0.01$; Figure 4-31).

In order to examine the efficacy of CQ in producing analgesia when the animals were stimulated by mechanical stimuli. Rats were injected i.p. NSS or various doses of CQ (43.5, 87.5, 175, 350, and 700 mg/kg). CQ doses of 175 mg/kg or higher significantly ($p< 0.05$, $p< 0.01$, $p< 0.01$, respectively) increased the area of analgesia when compared to NSS. (Figure 4-32).

When the log of the CQ dose was plotted versus the area of analgesia a significant linear correlation was observed. When all five doses of CQ (43.5, 87.5, 175, 350, and 700 mg/kg) were plotted, a linear correlation coefficient (r^2) equal to 0.99 was observed (Figure 4-34). The analgesic peak effect of CQ was reached within 60-90 min after i.p. administration in all CQ doses tested and individual time courses of the responses are shown in Figure 4-35.

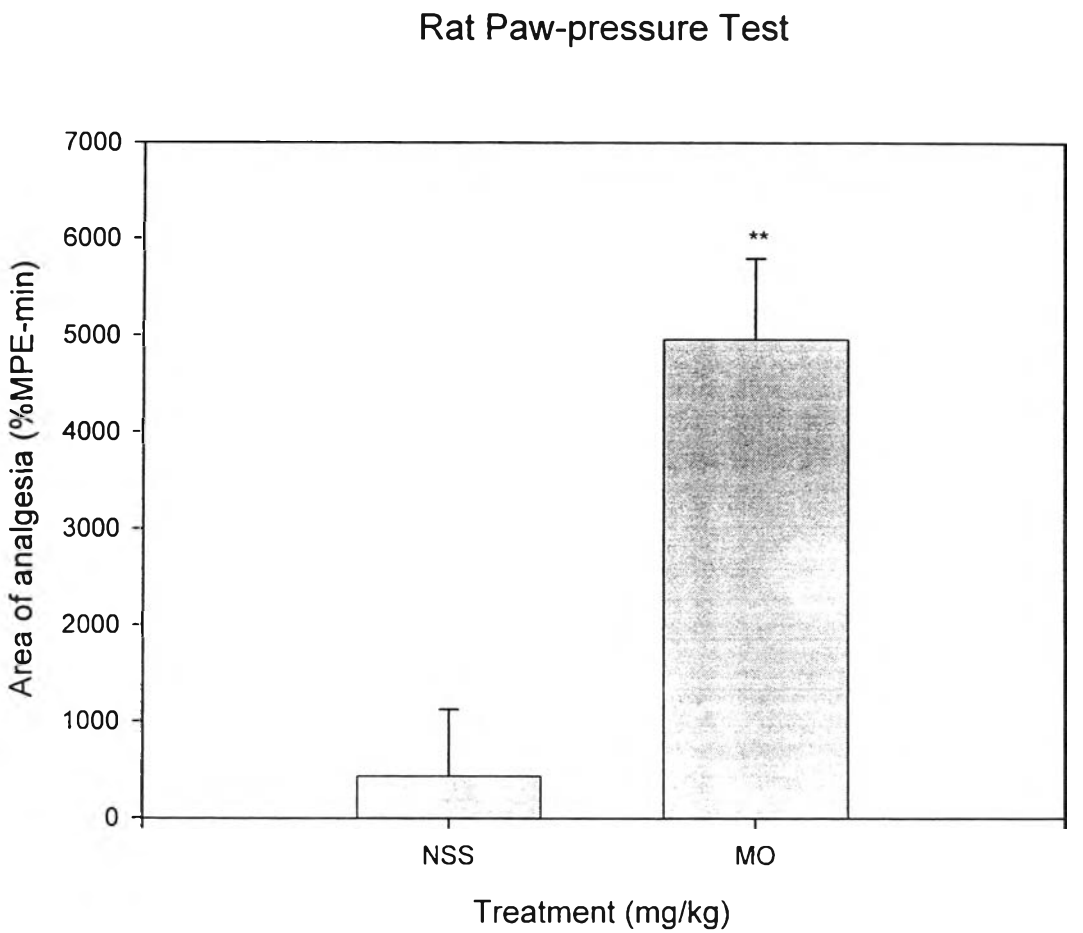

Figure 4-30 Area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS) and morphine sulphate (MO; 10 mg/kg). N=10 for all groups. ** $p< 0.01$ significantly different compared to NSS.

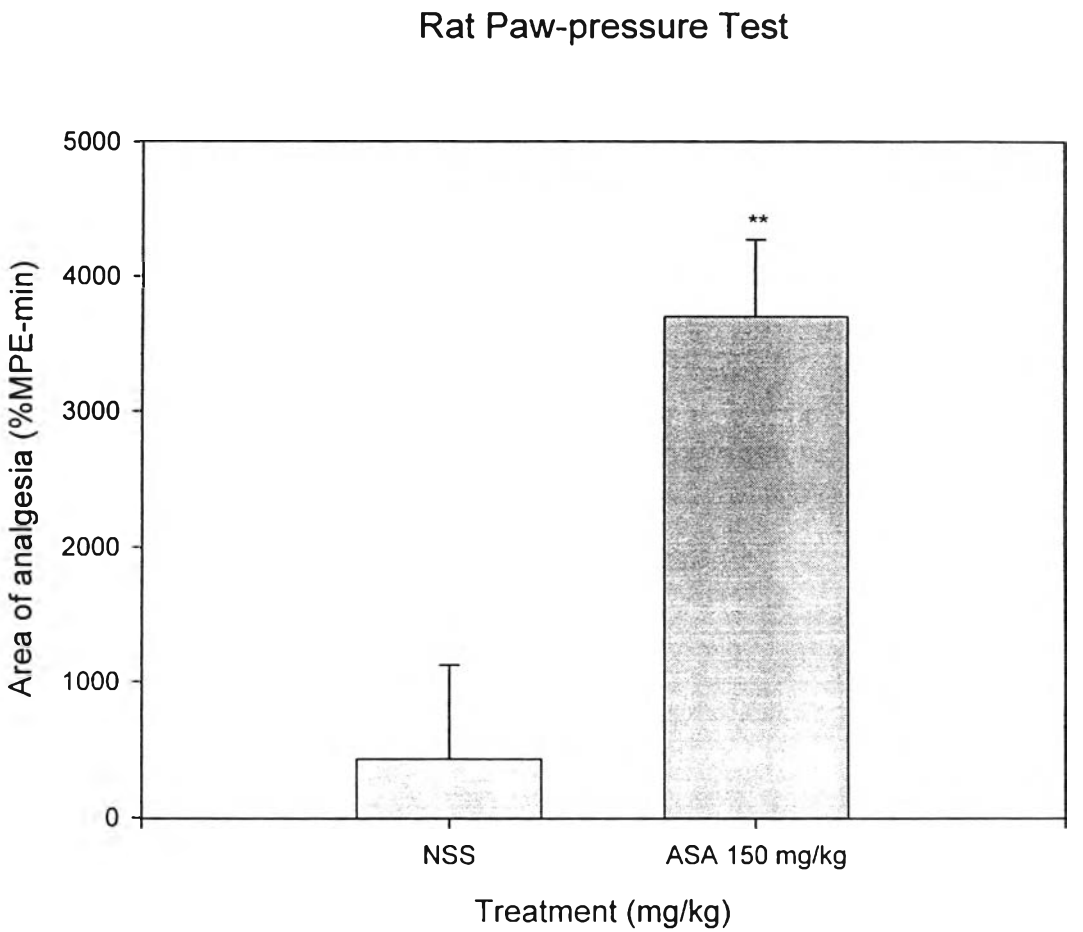

Figure 4-31 Area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS) and acetylsalicylic acid (ASA; 150 mg/kg) N=10 for all groups. ** $p < 0.01$ significantly different compared to NSS.

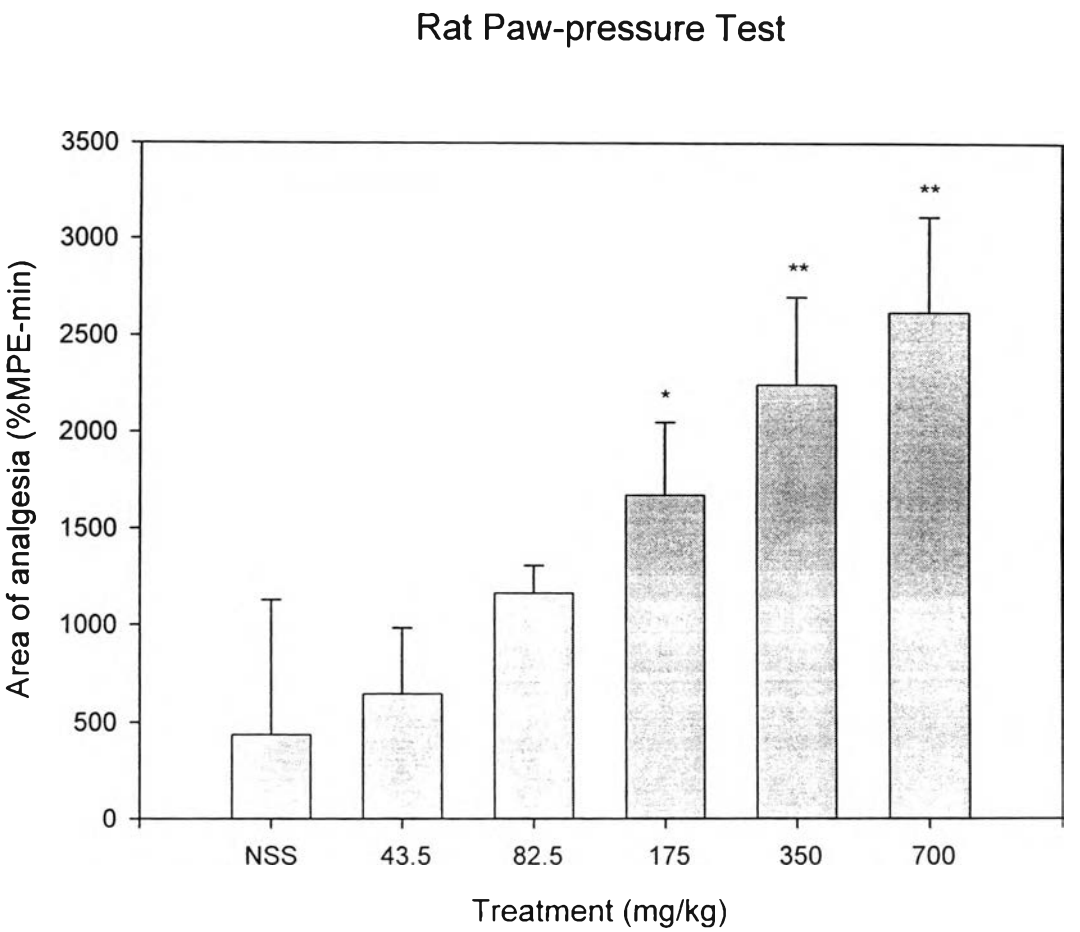

Figure 4-32 Area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS) and the crude extract of *C. quadrangularis* dried stems (CQ; 43.5-700 mg/kg). N=10 for all groups. * $p< 0.05$,** $p< 0.01$ significantly different compared to NSS.

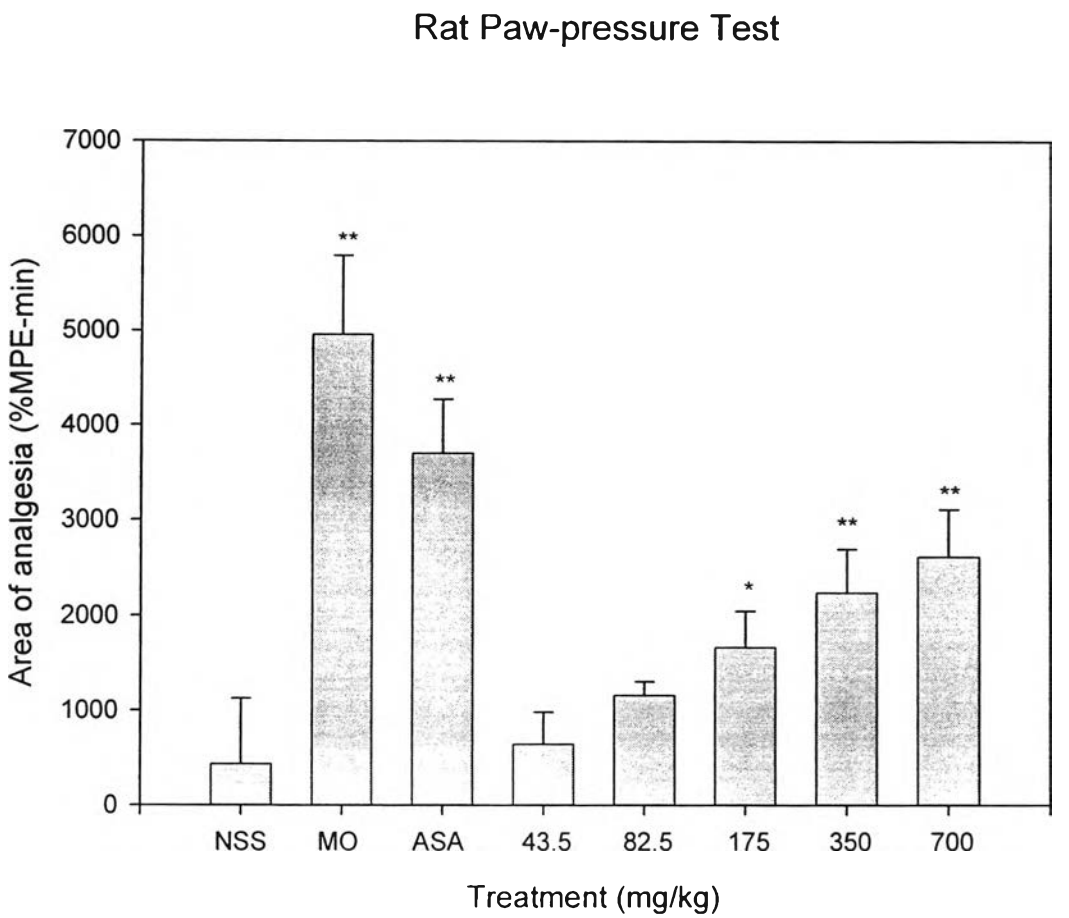

Figure 4-33 Area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS), MO (10 mg/kg), ASA (150 mg/kg) and various doses of CQ (43.5-700 mg/kg). N=10 for all groups. * $p < 0.05$,** $p < 0.01$ significantly different compared to NSS.

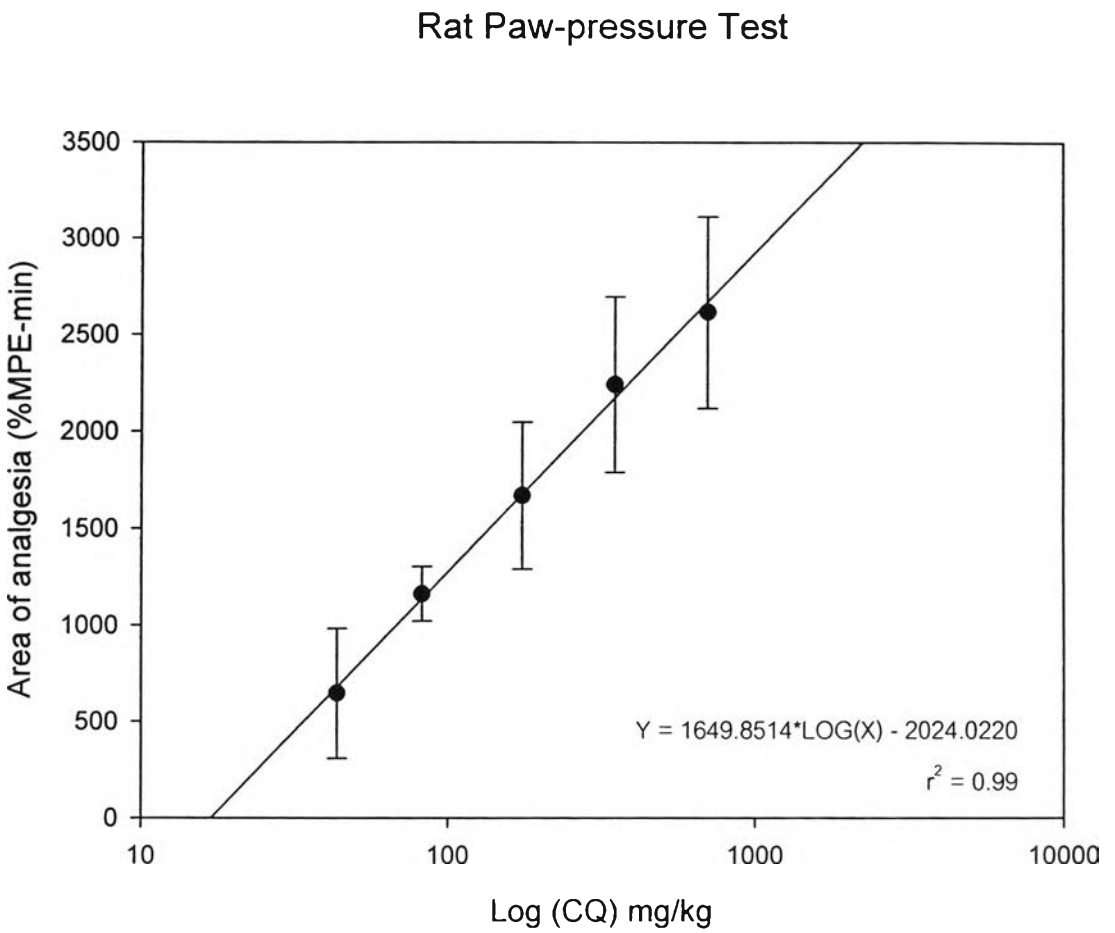

Figure 4-34 Linear regression of area of analgesia (%MPE-min) from 0-240 minutes after intraperitoneal administration of various doses of CQ (43.5-700 mg/kg). N=10 for all groups. The regression equation was Y = 1649.8514LOG(X) - 2024.0220 , r^2 =0.99

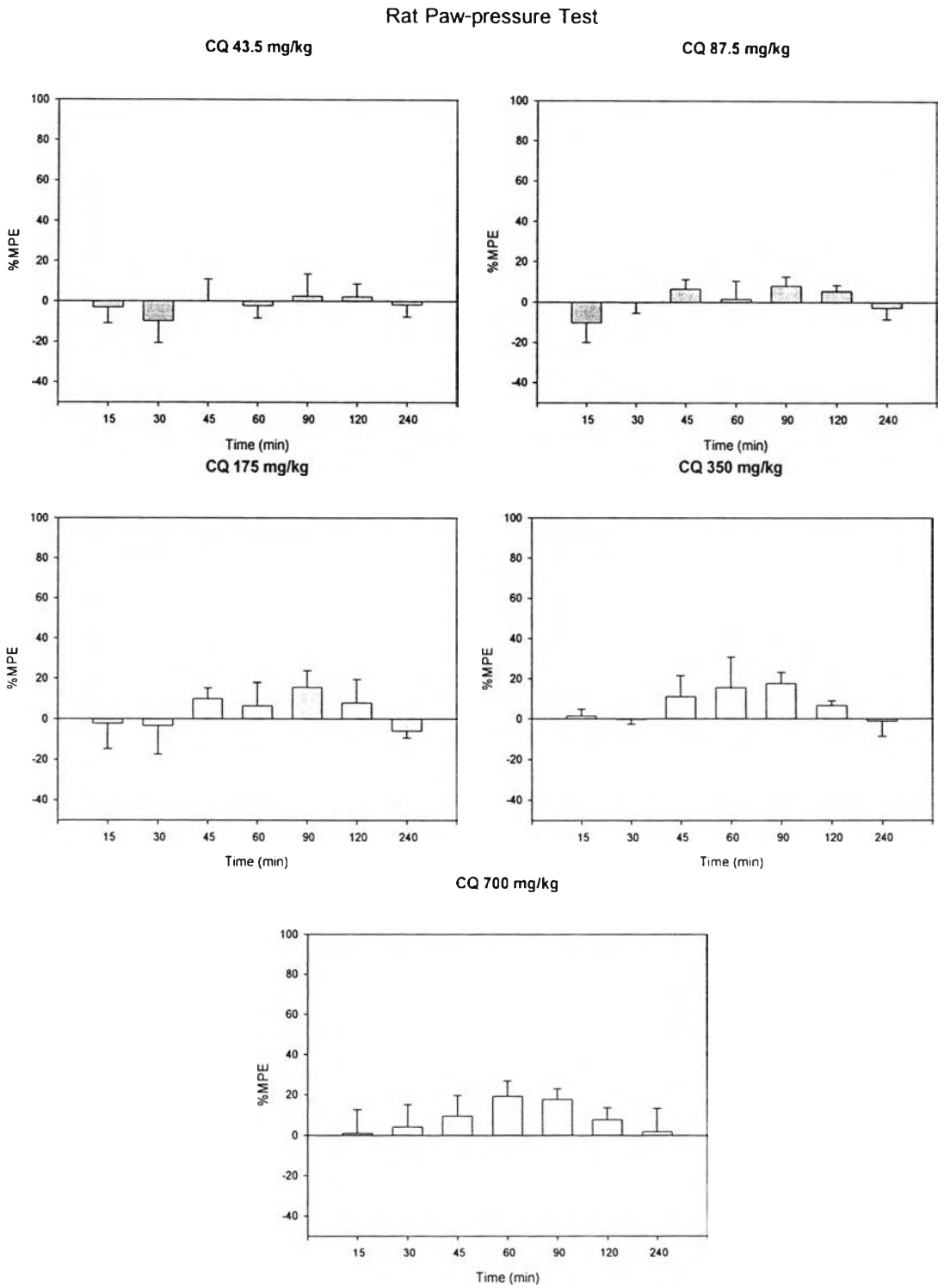

Figure 4-35 Individual time courses of the response (%MPE versus time (min)) after intraperitoneal administration of various doses of CQ (43.5-700 mg/kg). N=10 for all groups.

RAT INFLAMED PAW PRESSURE TEST

To determine the antihyperalgesic effect of CQ in carrageenan induced paw inflammation, the Randall Selitto paw pressure technique was used. Two hours after the carrageenan injection into the plantar surface of rat's right hind paw, the right hind paw was red and swollen. The contra-lateral, left hind paw appeared unaffected. In control group rats (receiving a systemic injection of 0.9%NSS i.p.), withdrawal threshold after mechanical stimulation of inflamed paw 40±27 g) were significantly shorter than the non-inflamed paw (49±9.7 g), indicating a carrageenan induced hyperalgesia.

To demonstrate the validity of the paw-pressure technique following i.p. drug administration, rats received morphine (MO; 10 mg/kg) or indomethacin (IND; 5 mg/kg) i.p. 30 min prior administering carrageenan, two hours later, rats were tested for mechanical hyperalgesia. MO significantly ($p<0.01$) increased pressure threshold compared to NSS (Figure 4-36). The i.p. administration of IND (5 mg/kg) also increased pressure threshold when compared to NSS ($p<0.01$; Figure 4-37).

To evaluate the antihyperalgesic effect of CQ, rats were received various doses of CQ (43.5, 87.5, 175, 350, and 700 mg/kg) i.p. 30 min before carrageenan administration. CQ doses of 350 and 700 mg/kg significantly ($p < 0.05$, $p < 0.01$, respectively) increased pressure threshold when compared to NSS. (Figure 4-38). All doses of CQ failed to exerted analgesic effect on both inflamed and intact paws when compared to NSS treated group. (Figure 4-39).

When the log dose of CQ was plotted versus the area of analgesia a significant linear correlation was observed. All five doses of CQ (43.5, 87.5, 175, 350, and 700 mg/kg) were plotted and a significant linear correlation coefficient (r^2) equal to 0.98 was observed (Fig.4-31).

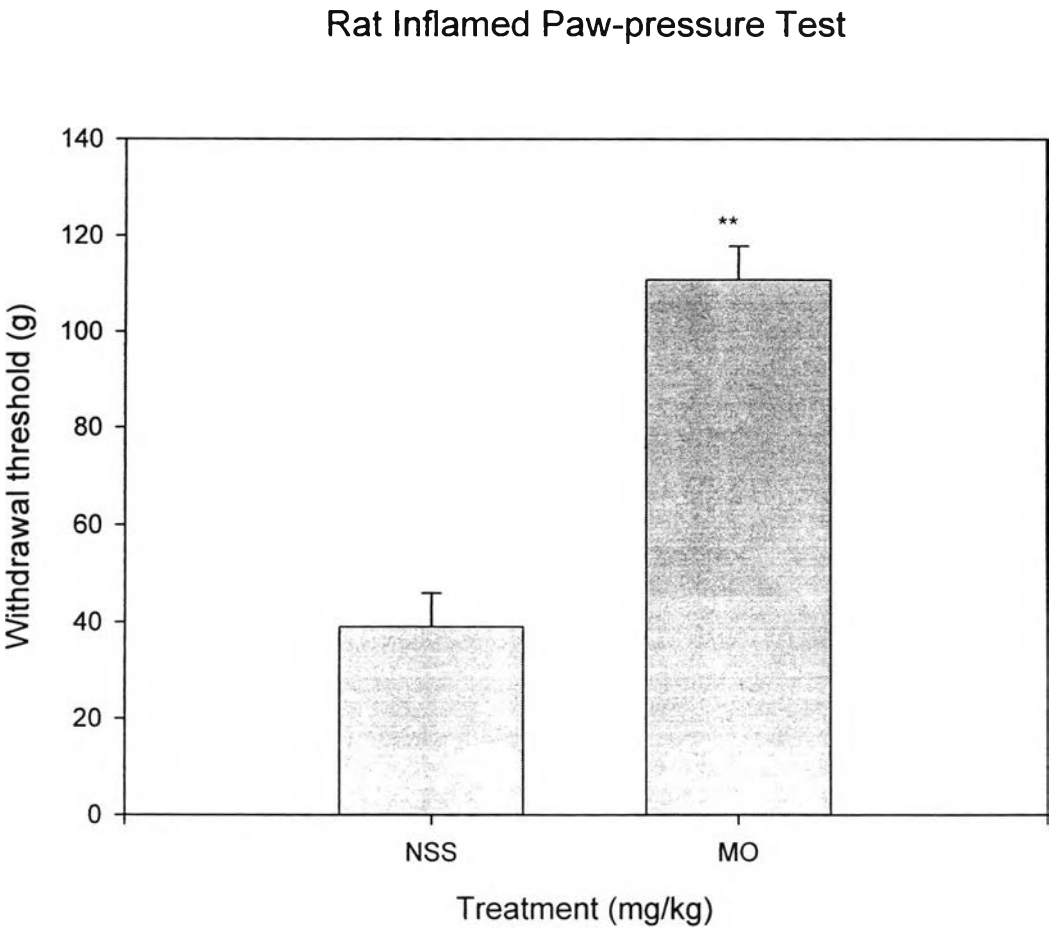

Figure 4-36 Withdrawal threshold pressure from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS) and morphine sulphate (MO; 10 mg/kg) N=10 for all groups. ** $p < 0.01$ significantly different compared to NSS.

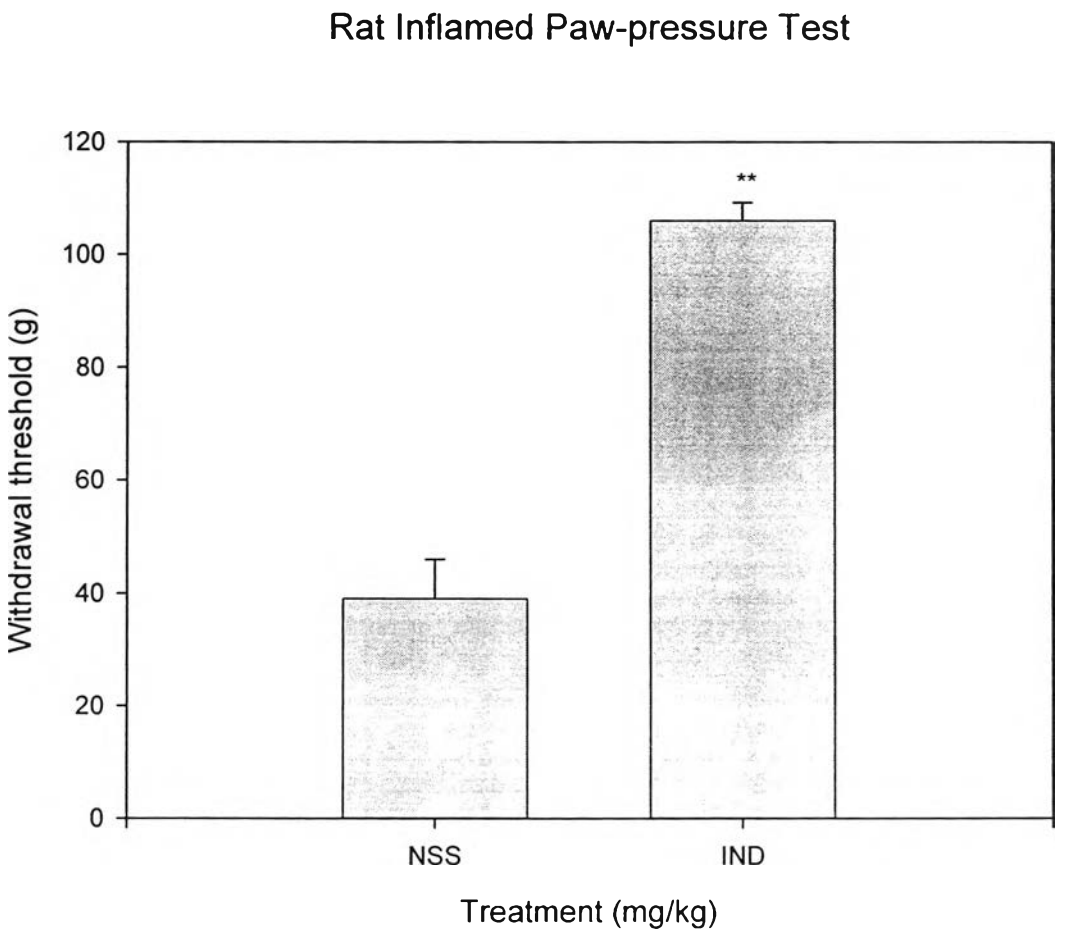

Figure 4-37 Withdrawal threshold pressure from 0-240 min after intraperitoneal administration of 0.9% normal saline solution (NSS) and indomethacin (IND; 5 mg/kg) N=10 for all groups. ** $p < 0.01$ significantly different compared to NSS.

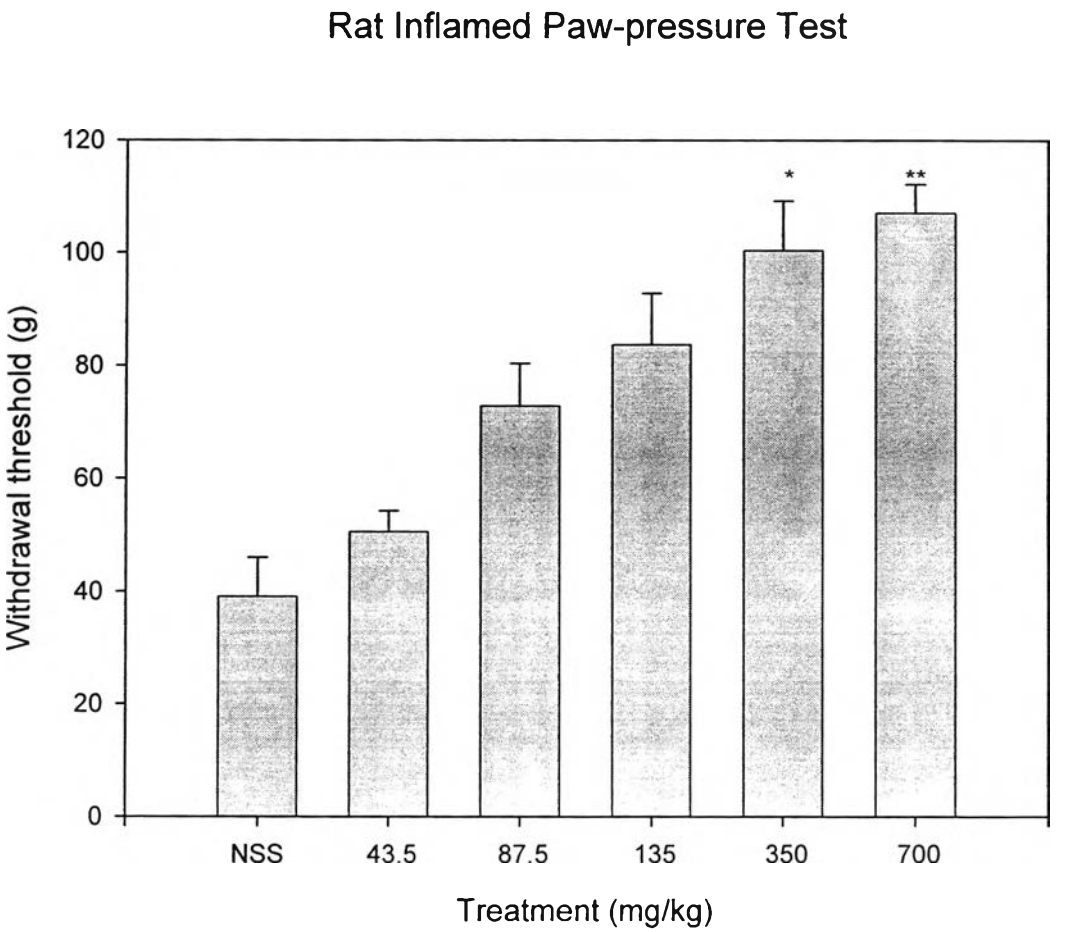

Figure 4-38 Withdrawal threshold pressure from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS) and various doses of the crude extract of *C. quadrangularis* dried stems (CQ; 43.5-700 mg/kg), N=10 for all groups. * $p< 0.05$,** $p< 0.01$ significantly different compared to NSS.

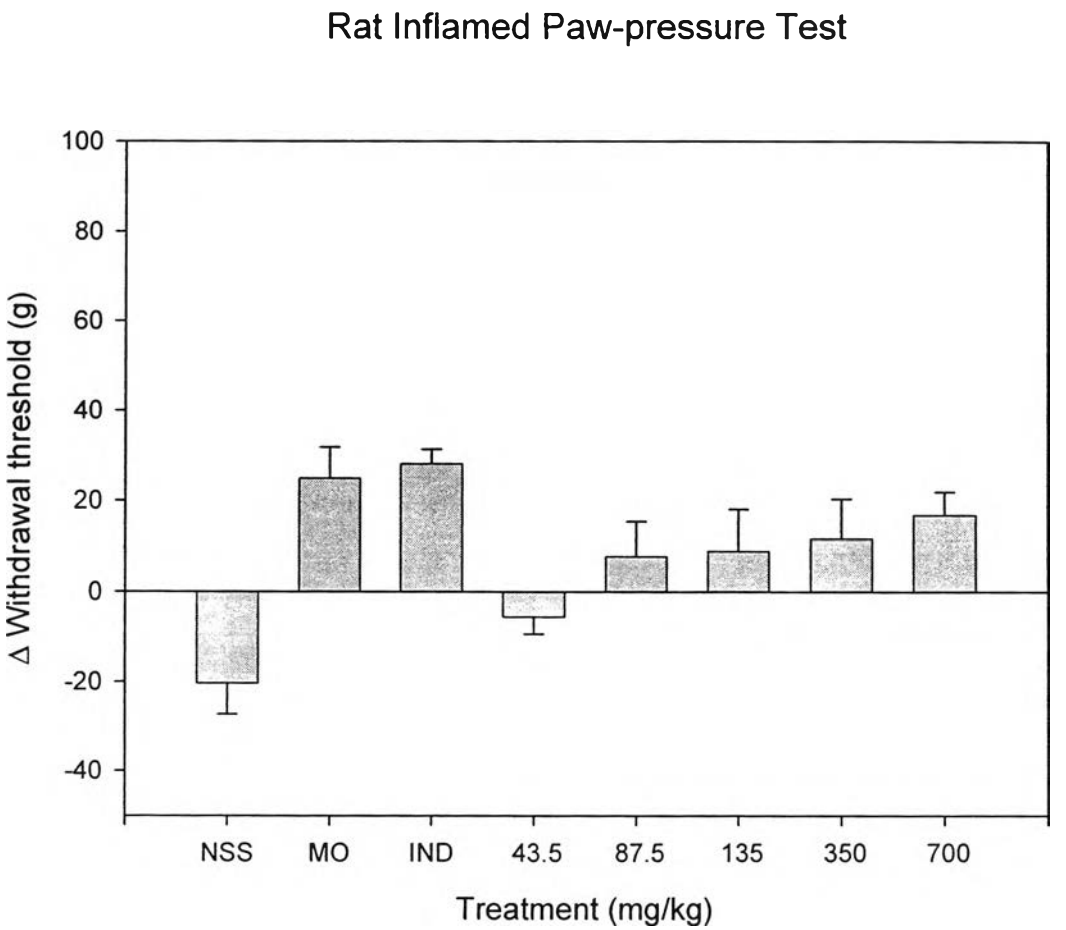

Figure 4-39 Δ Withdrawal threshold pressure from 0-240 minutes after intraperitoneal administration of 0.9% normal saline solution (NSS), MO (10 mg/kg), IND (5 mg/kg) and various doses of CQ (43.5-700 mg/kg). N=10 for all groups.

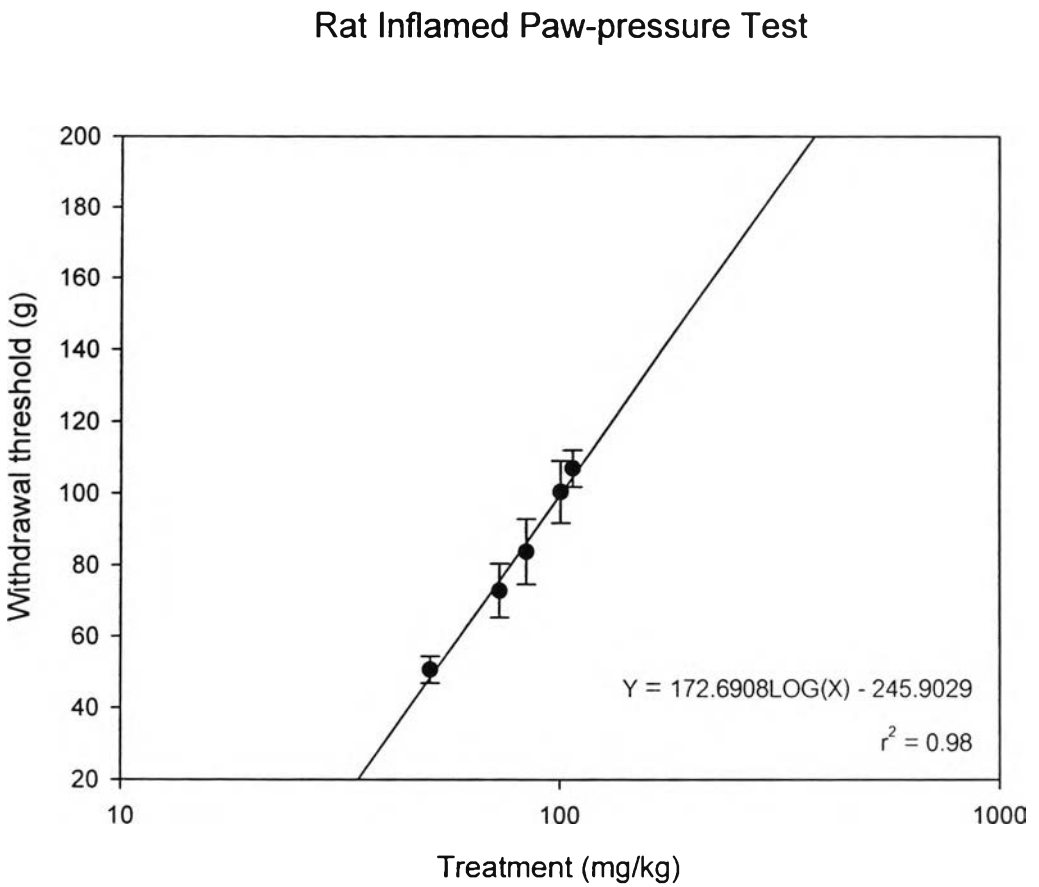

Figure 4-40 Linear regression of paw withdrawal threshold from 0-240 minutes after intraperitoneal administration of various doses of CQ (43.5-700 mg/kg). N=10 for all groups. The regression equation was Y = 172.6908LOG(X) - 245.9029, r^2 = 0.98