## RESULTS

The concentration-response curves and mean increase in maximum responses of heart rate, mean arterial blood pressure and contractile force (tension) to norepinephrine, epinephrine, isoproterenol and dopamine in isolated rat atrial preparations and anesthetized rats of control, morphinedependent and morphine-withdrawal groups were illustrated and summarized in Figure 1 - 8 and Table 1, respectively.

Norepinephrine at concentrations of  $3 \times 10^{-4}$  and  $10^{-3}$  M;  $10^{-4}$ ,  $3 \times 10^{-4}$  and  $10^{-2}$  M significantly increased and decreased heart rate (P < 0.05 and 0.01) in morphine-dependent and morphine-withdrawal isolated rat atrial preparations, respectively, whereas norepinephrine at a concentration range of  $10^{-3}$  -  $3 \times 10^{-2}$  M significantly increased only tension (P < 0.05 and 0.01) in the morphine-dependent group (Fig. 1)

Epinephrine at concentrations of  $10^{-2}$  and 3 x  $10^{-2}$  M significantly decreased heart rate in morphine-withdrawal isolated rat atrial preparations (P < 0.01) but produced no significant changes in responsiveness of tension in both morphine-dependent and morphine-withdrawal isolated rat atrial preparations when compared with the control group (Fig. 2).

Isoproterenol at concentrations of  $3 \times 10^{-6}$  and  $10^{-5}$  M;  $3 \times 10^{-5}$  and  $10^{-4}$  M significantly increased and decreased heart rate (P < 0.05 and 0.01) in morphine-dependent and morphine-withdrawal isolated rat atrial preparations, respectively, while isoproterenol ( $3 \times 10^{-5} - 3 \times 10^{-2}$  M) significantly increased tension (P < 0.05 and and 0.01) only in morphine-dependent isolated rat atrial preparations compared with the control group (Fig. 3).

Dopamine at a concentration range of  $3 \times 10^{-3}$  -  $3 \times 10^{-2}$  M significantly decreased heart rate (P < 0.05 and 0.01) in morphine-withdrawal isolated rat atrial preparations, while dopamine at concentrations of  $10^{-2}$  and  $3 \times 10^{-2}$  M caused a significant increase of tension (P < 0.05 and 0.01) in morphine-dependent isolated rat atrial preparations compared with the control group (Fig. 4).

In addition, norepinephrine, isoproterenol and dopamine but not epinephrine significantly increased maximum responses of tension (P < 0.01) in the isolated atria of chronic morphine-treated rats, whereas norepinephrine, epinephrine and dopamine but not isoproterenol significantly decreased maximum responses of heart rate (P < 0.05) and (0.01) in the morphine-withdrawal rats compared with normal rats (Table 1).

## Anesthetized rats

Norepinephrine at concentrations of  $3 \times 10^{-6}$  and  $10^{-5}$  M;  $10^{-6}$  -  $10^{-5}$  M produced a significant increase in heart rate (P < 0.01) and mean aterial blood pressure (P < 0.05 and 0.01) only in the chronic morphine-dependent group (Fig. 5)

Epinephrine at only specific concentrations exhibited a corresponding increase and decrease of heart rate and mean arterial blood pressure (P < 0.01) in chronic morphine-treated and morphine-withdrawal rats, respectively compared with normal saline-treated rats (Fig. 6).

Isoproterenol at a concentration range of  $10^{-8}$  -  $10^{-5}$  M and 3 x  $10^{-8}$  -  $10^{-5}$  M produced a markedly significant increase of heart rate (P < 0.01) and decrease of mean arterial blood pressure (P < 0.01), respectively in both chronic morphine-treated and morphine-withdrawal rats compared with control rats (Fig. 7).

Dopamine (3 x  $10^{-5}$  -  $10^{-3}$  M) exhibited only a significant increase of mean arterial blood pressure (P < 0.05 and 0.01) in chronic morphine-treated rats compared with normal anesthetized rats (Fig. 8).

In addition, norepinephrine, epinephrine and isoproterenol except dopamine significantly increased maximum responses of heart rate in anesthetized rats of chronic morphine-treated rats, whereas epinephrine and isoproterenol produced a significant increase of maximum responses of heart rate (P < 0.01) in morphine-withdrawal rats. Moreover, norepinephrine and dopamine significantly increased maximum responses of mean arterial blood pressure (P < 0.05 and 0.01) in morphine-dependent rats, whereas isoproterenol significantly decreased only maximum responses of mean arterial blood pressure (P < 0.01) both in morphinedependent and morphine-withdrawal rats compared with normal rats (Table 1).