
SUMMARY AND CONCLUSION

Carvedilol is a B-adrenoceptor–antagonist drug with α_1 -adrenoceptor–antagonist activity with potent antioxidant property. On the other hand valsartan is a selective AT1 receptor antagonist.

The present work was carried out to screen the pharmacological effects of carvedilol and valsartan on isolated rabbit aortic strip and isolated rabbit heart. Also, the effects of carvedilol versus valsartan on isoprenaline induced heart failure in rats were evaluated.

Moreover the cardioprotective effects of carvedilol and valsartan on isoprenaline induced acute myocardial infarction in rats were studied.

Data obtained in the present study pointed out that carvedilol antagonized norepinephrine and had no effect on angiotensine II induced contractions in isolated rabbit aortic strip and produced insignificant dose dependent reduction of basal myocardial contractility on isolated rabbit heart.

On the other hand, valsartan in gradually increasing doses produced no effect on adrenaline induced aortic contraction.while, valsartan in gradually increasing doses produced significant decrease in amplitude of angiotensin II induced contraction in isolated rabbit aorta. Valsartan in gradually increasing doses produced no effect on amplitude of myocardial contractility of isolated rabbit heart, but significantly reduced the positive inotropic effect of Ang II on isolated rabbit heart.

Heart failure was experimentally induced in rats by a single S.C injection of isoprenaline. After 4 weeks, there was significant decrease in

the systolic and mean arterial blood pressure. Also, there was no significant difference in the heart rate in compared with control group.

In the present work, it was observed that daily oral administration of carvedilol 1mg/kg and valsartan 3 mg/kg for 4 weeks produced significant reduction in arterial blood pressure but produced insignificant decrease in H.R. when compared with H.F. group. And there was insignificant difference between effects of both drugs.

Histopathological examination of cardiac sections of control group showed no detectable abnormality in cardiac smooth muscle cells. Sections of heart failure group revealed myocyte degeneration and necrosis and interstitial fibrosis. Carvedilol and valsartan administration effectively decreased these changes.

The degree of cardio-protective effect induced by carvedilol and valsartan was evaluated by studying the changes in the severity of the cardiac necrosis evoked by isoprenaline in rats. It was found that carvedilol and valsartan treatment did not minimize the infarction size and there was no significant difference in myocardial infarction size between the 3 groups.

Myocardial infarction was experimentally induced by subcutaneous injection of isoprenaline. The electrocardiograph tracing showed sinus tachycardia with injury currents in form of highly peaked T-wave, serum creatine phosphokinase CPK level increased in rats 4 hours after subcutaneous injection of isoprenaline and the mean percentage of infarction size was (38.9 ± 0.09) and histopathological

examination of cardiac sections of control group revealed myocyte degeneration and necrosis and interstitial fibrosis.

Pre-treatment and post-treatment with carvedilol decreased significantly the T- wave voltage and levels of CPK. However, produced insignificant decrease in heart rate. on the other hand, pre-treatment and post treatment with valsartan decreased significantly the T- wave voltage and levels of CPK. However, produced insignificant decrease in heart rate and myocardial infarction size. And there were significant difference between the 4 groups.

In conclusion, carvedilol decreased norepinephrine, and had no effect on Ang II induced contractions in isolated rabbit aortic strip. Also, it insignificantly inhibited basal myocardial contractility but significantly reduced the positive inotropic action of isoprenaline on the isolated rabbit heart. On the other side valsartan had no effect on norepinephrine induced contractions in isolated aortic strip but valsartan decreased the angiotensin II induced contraction in isolated rabbit aortic strip. Furthermore, valsartan did not modify the inotropic property of the isolated rabbit heart but significantly reduced the positive inotropic action of angiotensin II on the isolated rabbit heart. Furthermore, carvedilol and valsartan produced a protective effect on isoprenaline induced heart failure and acute myocardial infarction in rats.

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