7.0 SUMMARY & CONCLUSION

The present study was carried out to study the interaction of angiotensin converting enzyme inhibitors (ACEIs) enalapril and lisinopril, and concomitantly administered diclofenac sodium in non-diabetic and diabetic hypertensive arthritic patients.

On the basis of the results obtained from the effect of ACEIs as well as its concurrent administration with diclofenac sodium on various parameters, following observations were made:

1. Treatment with both enalapril and lisinopril significantly reduced both systolic and diastolic blood pressure in diabetic as well as non-diabetic patients. But, on concomitant treatment with diclofenac sodium, both the ACEIs lost blood pressure control significantly.

2. Insulin sensitivity was significantly enhanced in patients receiving chronic treatment with enalapril or lisinopril. Combining diclofenac sodium with enalapril or lisinopril counteracted the enhancement of insulin sensitivity shown by any of the ACEIs.

3. Urinary albumin excretion has been reduced following chronic treatment with enalapril or lisinopril. However, urinary albumin excretion was found to increase in patients receiving diclofenac sodium and either of the ACEIs under study when compared with those receiving either of the ACEIs but not diclofenac sodium.

4. There was no significant alteration found in percent platelet aggregation in patients receiving chronic enalapril or lisinopril treatment when compared with the values of their respective pre-treatment stage. However, percent platelet aggregation was significantly reduced in patients receiving diclofenac sodium along with enalapril or lisinopril when compared with those receiving enalapril or lisinopril alone.

5. In the present study, no significant change was observed in serum sodium level in the diabetic/non-diabetic patients receiving chronic enalapril or lisinopril treatment. Significant reduction in serum sodium levels were
observed in patients treated with combination of diclofenac sodium and enalapril or lisinopril.

6. Serum potassium level increased in patients on chronic ACEI (enalapril or lisinopril) therapy when compared with the baseline values and in patients receiving chronic treatment with either of the two ACEIs plus diclofenac sodium when compared with the long-term respective ACEI therapy in hypertensive patients with or without diabetes mellitus.

7. Serum creatinine as well as blood urea nitrogen (BUN) levels increased significantly in patients receiving ACEI and diclofenac sodium when compared with those on chronic ACEI treatment alone.

8. Serum cholesterol, serum triglycerides, serum HDL and serum LDL levels were not significantly altered in either diabetic or non-diabetic patients on chronic enalapril and lisinopril therapy.

9. Combined treatment with diclofenac sodium and lisinopril effectively reduced serum cholesterol level in both diabetic and nondiabetic patients. Significant reduction in serum triglyceride levels were also observed in diabetic patients treated with this combination.

10. Combined treatment with diclofenac sodium and enalapril showed significant reduction in serum triglyceride level in both non-diabetic and diabetic patients. This combination also showed significant reduction in serum LDL level in diabetic patients.

11. Concomitant treatment with diclofenac sodium and either of the ACEIs showed significant rise in serum HDL levels.

12. Serum LDL/HDL and serum cholesterol/HDL ratios decreased significantly upon treatment with either of the ACEIs combined with diclofenac sodium.

13. Concomitant treatment with diclofenac sodium and enalapril or lisinopril showed significant increase in SGOT activities in diabetic patients as compared to those treated with the respective ACEI alone. Although these changes were statistically significant, they were not clinically significant.

Based on our findings, it can be concluded that concomitant administration of diclofenac sodium with ACEIs (enalapril / lisinopril) has beneficial effect on lipid profile, insulin sensitivity, and platelet aggregation. On the other hand, the
antihypertensive efficacy of the ACEIs and renal function of the patients may be adversely affected by inclusion of diclofenac sodium in the therapy with ACEI. Although hepatic function was not affected with the use of the combination of diclofenac sodium and ACEI to the extent of clinical significance, periodic monitoring of hepatic function may be indicated on the basis of earlier reports of hepatotoxicity with ACEIs. Serum potassium and serum sodium levels were also altered without demonstrating any clinical symptoms, but close monitoring of the patients for any signs and symptoms of hyponatremia and hyperkalemia is necessary. It can also be suggested that blood pressure and renal function may be closely monitored in hypertensive arthritic patients (with or without diabetes mellitus) receiving NSAID and ACEI combination.

For the practicing physician, it is wise to balance the risk of an increase in blood pressure against the expected benefit of treatment with an NSAID. In patients with hypertension and in the elderly, the benefits may not always outweigh the admittedly small risk. Should the physician decide to prescribe an NSAID, frequent measurement of blood pressure may be necessary during the first weeks of treatment. There seems to be an antagonism between diclofenac sodium and ACEIs in hypertensive patients with diabetes. This interaction would have both biologic and public health implications. However, the negative interactions observed in our study suggest that adding diclofenac sodium to patients on ACEIs may not be beneficial. On the other hand, the positive interactions observed in our study favour addition of diclofenac sodium to the arthritic hypertensive patients' ongoing therapeutic regimen of either of the two ACEIs. However, more research is needed to confirm the interaction found in this study, clarify the mechanisms involved, and to discover whether diclofenac sodium may be replaced by safer NSAIDs.