

CONTENTS

	page
LIST OF FIGURES	iv
LIST OF TABLES	vii
ABSTRACT	viii
INTRODUCTION	1
MATERIALS AND METHODS	13
Materials	13
Methods:	
1. Preparation of metacercarial cysts of <i>O. viverrini</i>	14
2. Infection of animal host	15
3. Extraction of free proline and collagen from the liver	15
4. Determination of proline and hydroxyproline	17
5. Protein determination	17
6. Preparation of [³ H]-procollagen substrate	18
7. Liver prolyl hydroxylase activity assay	19

8.	Incorporation of [³ H]-proline or [¹⁴ C]-glutamine or [¹⁴ C]-arginine into the liver slices	20
9.	Turnover of hepatic collagen in normal and infected livers	21
10.	Effect of praziquantel treatment on prolyl hydroxylase activity and collagen content in the infected liver	21
RESULTS:		23
1.	The effect of <i>O. viverrini</i> infection on the wet weight, protein and collagen content of hamster liver	23
2.	Assay of prolyl hydroxylase activity in normal and infected livers	23
3.	The relationship between liver collagen content, prolyl hydroxylase activity and the infection time	26
4.	Effect of degree of infection on the prolyl hydroxylase activity	31
5.	Biosynthesis of collagen in the liver slices	31
6.	Pool sizes of free prolyl in normal and infected livers	36

7. Proline precursors	39
8. Turnover of collagen in the <i>O. viverrini</i> infected and normal liver	39
9. Effect of praziquantel treatment on collagen content and prolyl hydroxylase level in the <i>O. viverrini</i> infected liver	47
DISCUSSION	55
SUMMARY	66
REFERENCES	67

ABSTRACT

The histopathological studies in the liver infected by *Opisthorchis viverrini* have indicated liver fibrosis which resulted in deterioration of liver functions. This finding has drawn our interests toward the effect of *opisthorchiasis* on hepatic collagen metabolism. Our results showed an increase in liver collagen content as well as prolyl hydroxylase activity which is required in the process of collagen biosynthesis in the infected liver. The results therefore suggested some alteration in collagen metabolism in *O. viverrini* infected liver.

In this study, the pattern of increase in liver collagen content, liver prolyl hydroxylase activity, and free proline content was determined at various times (1-24 weeks) after infection. The pattern of increase in collagen content was similar to that of the enzyme activity. Both parameters increased at the early stage of infection but no further increase was observed at long infection time. However, the increase of both collagen content and prolyl hydroxylase activity did not correlate with that of proline pool size in the infected liver. Therefore, the possibility that the biosynthesis of collagen might be controlled by free proline pool seemed to be unlikely. The *in vitro* biosynthesis of collagen by measuring the incorporation of [^3H]-proline into liver collagen by using liver slices also showed an enhancing in hepatic collagen synthesis in infected hamster. Both results suggested that the rate of collagen synthesis was stimulated in *Opisthorchiasis* resulting

in the formation of hepatic fibrosis.

The turnover rate of collagen in the *Opisthorchis* infected liver was studied and compared to that of normal liver. There was an approximately 2 fold increase in the rate of degradation of newly synthesized collagen in the infected liver. Thus, it appeared unlikely that the increase in collagen content in the infected liver was due to a decrease in its degradation rate.

Praziquantel, a new series of anthelmintic drug was also found to be effective against *opisthorchiasis*. The liver fibrosis was recovered after praziquantel treatment since no stimulating of collagen synthesis occurred after eradication of the liver fluke.