

SPECULATIVE STUDIES ON AN ANOMERIC SPECIFICITY OF INDUCERS OF D-LYXOSE ISOMERASE

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1. Introduction

We have previously reported that *Mycobacterium smegmatis* seems to be unusual among microorganisms in that the inducer specificity of pentose isomerases is relatively broad [1]. We assumed that the configuration necessary for the induction of D-ribose isomerase is the configuration of C-1 to C-3 of D-ribose. Also the configuration of C-2 to C-4 of L-arabinose seemed to be essential for the induction of L-arabinose isomerase. D-Lyxose isomerase, however, was induced by D-lyxose and D-mannose, and D-ribose, dulcitol and myo-inositol were also shown to serve as inducers for the enzyme. Thus, it was not clear from these results what is the essential structure for the induction of D-lyxose isomerase. In this paper, by comparison of molecular models of these compounds, taking into consideration the configuration of OH groups, we discuss the essential structure of the inducer of D-lyxose isomerase in *Mycobacterium smegmatis*.

2. Discussion

The substrates of D-lyxose isomerase are D-lyxose and D-mannose [2,3] and the enzyme catalyzes the first reaction in the metabolism of both sugars [4]. D-Ribose isomerase is the first enzyme of the metabolism of D-ribose and was induced by D-ribose, and D-lyxose isomerase also was induced by D-ribose gratuitously [5,6]. The reason why D-ribose induced D-lyxose

isomerase seemed to be a mystery. It is easy to find a common configuration between D-lyxose and D-mannose, namely the configuration of C-1 to C-4 of both sugars are the same (fig.1). The configuration of D-ribose, however, seems to have almost nothing in common with that of D-lyxose and D-mannose.

From the results showing that L-arabitol and dulcitol were inducers of the L-arabinose isomerase, and that inositol could not induce the enzyme [1], it seems likely that the open chain form of the inducers was effective for the enzyme induction. In contrast to the results of L-arabinose isomerase, D-lyxose isomerase was not induced by D-arabitol and D-mannitol, but was induced by myoinositol. Thus, it is assumed that an α - or β -form of D-lyxose is effective for the D-lyxose isomerase induction. Under the assumption that there must be a common structure between various inducers for enzyme induction we attempt to deduce the common structure of various inducers of D-lyxose isomerase and consequently the essential configuration.

As shown in fig.1, D-xylose, which is not an inducer

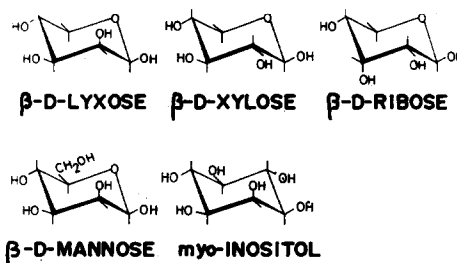


Fig.1. The structures (β , C-1) of various inducers of D-lyxose isomerase and D-xylose.

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of D-lyxose isomerase, has almost the same configuration as D-lyxose except the OH group at C-2. On the other hand, D-ribose which can induce the enzyme has different configurations at the C-2 and C-3. Taking into consideration the results which showed that myo-inositol with no oxygen atom in the ring is an inducer of the enzyme, it is assumed that the oxygen atom in the pyranose ring of D-lyxose is not essential for the enzyme induction, whereas OH groups at four carbons has essential roles in inducing the enzyme. These results suggest that in fig.1, the carbons of the pyranose ring of D-lyxose and D-ribose are not placed in a suitable position to produce a common configuration between them.

We found unexpectedly that we could overlap all OH groups of β -D-ribose with those of β -D-lyxose completely when the β -D-ribose was rotated around a certain axis by 180° as shown in fig.2. The four OH groups at the C-4 to C-1 of β -D-ribose are completely overlapped with those of the C-1 to C-4 of β -D-lyxose, respectively. This finding seems to suggest the reason why D-ribose induced D-lyxose isomerase gratuitously.

Of all the pentoses examined in induction experiments, D-ribose was the only pentose that could induce D-lyxose isomerase except D-lyxose. There must be a specific relationship between D-lyxose and D-ribose. Accordingly to propose that the configuration of β -D-lyxose is the essential structure for the enzyme induction, we must prove two things:

- (i) None of the pentoses overlap on β -D-lyxose except β -D-ribose.

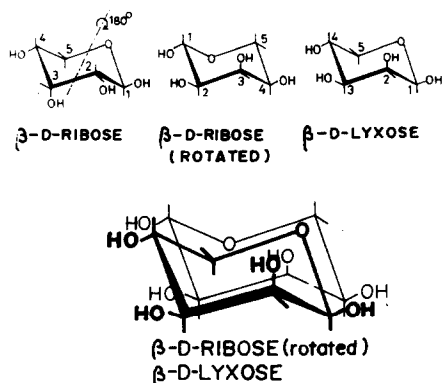


Fig.2. Overlapping of β -D-ribose on β -D-lyxose. β -D-Ribose was rotated around the axis (---) by 180° and overlapped on β -D-lyxose.

COMPOUND	STRUCTURE (C-1)			
	α -Form		β -Form	
	Group A	Group B	Group A	Group B
D-LYXOSE				
L-LYXOSE				
D-ARABINOSE				
L-ARABINOSE				
D-RIBOSE				
L-RIBOSE				
D-XYLOSE				
L-XYLOSE				

Fig.3. Conformational structures of eight pentoses in pyranose form (C-1). The compounds of Group B depict forms which arise by rotating the pyranose ring in Group A around a certain axis by 180° as done for β -D-ribose in fig.2.

- (ii) α - or β -D-Ribose do not overlap on β -D-lyxose.

The compounds of Group B of fig.3 depict forms which arise by rotating the configurations of Group A by 180° as done for β -D-ribose in fig.2. By comparison of various pentoses with the aid of fig.3, we can discuss about the problems (i) and (ii) mentioned above.

- (i) All of OH groups of β -D-ribose (Group B) overlap with the OH groups of β -D-lyxose as shown in fig.2 and of the seven pentoses β -D-ribose is the only pentose which exhibits this overlap with β -D-lyxose.
- (ii) By the same way, we can fit all of OH groups of β -L-lyxose (Group B) on α -D-lyxose but any other pentoses including α - and β -D-riboses can not be overlapped on α -D-lyxose. Considering L-lyxose is not an inducer of D-lyxose isomerase, the results obtained suggest strongly that β -D-lyxose is an effective form for the enzyme induction.

The role of the OH groups at a certain carbon may be assessed from a comparison of structures of pentoses, taking into consideration the configuration of each OH group and the ability for the enzyme induction. Thus, it is assumed that of four OH groups of D-lyxose, three of them at C-1, C-2 and C-3 might be essential because L-lyxose (β -form in the Group B), D-xylose (β -form in the Group A) and D-arabinose (β -form in the Group A) were not effective for the enzyme induction respectively [1]. At the present time, we can not use L-ribose for induction experiments, so it is less clear whether the OH group at C-4 of D-lyxose is essential or not. The reason why dulcitol induces the enzyme is not clear. However, we suggest that the configuration of dulcitol in the solution happens to be similar to β -D-lyxose.

By a comparison of inducers similar to that made for the D-lyxose isomerase, we are able to discuss the essential forms of D-xylose and D-ribose isomerases in *Mycobacterium smegmatis*. D-Xylose isomerase is induced only by D-xylose [1]. We found that only one pentose, L-arabinose (β -form in Group B) maybe overlapped on D-xylose (α -form in Group A) completely as is the case of β -D-ribose and β -D-lyxose, but L-arabinose has no ability to induce D-xylose isomerase. Thus, it may be concluded that β -D-xylose on which none of the seven pentoses overlap, is the effective inducer form and all OH groups at C-1, C-2, C-3, and C-4 are essential for D-xylose isomerase induction. D-Ribose isomerase is induced by D-ribose and L-lyxose [6]. We can overlap L-ribose (β -form in the Group B) and D-lyxose (β -form

in the Group B) on α - and β -D-riboses, respectively. Also, L-ribose (α -form in the Group B) and D-lyxose (α -form in the Group B) overlap on α - and β -L-lyxoses, respectively. The results of the induction experiments suggest that although D-lyxose may be overlapped with both inducers, D-ribose and L-lyxose, it itself could not induce the enzyme. From these results we can deduce that α -D-ribose is the effective inducing configuration and OH groups at C-1, C-2 and C-3 may be essential for induction.

Such methods used in this paper to study the essential structure for the induction of D-lyxose isomerase are speculative, but we believe that these kind of studies will provide a new clue to the mechanism of enzyme induction.

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