

α -D-Mannosidase β -D-Mannosidase

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Activities of α -D-Mannosidase and β -D-Mannosidase in Patients with Liver Diseases

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Background/Aims: We studied the activities of α - and β -D-mannosidase to evaluate their diagnostic significance in liver diseases. **Methods:** One hundred fifty one patients with liver diseases were enrolled. The activities of the enzymes were measured by microquantitative spectrophotometry. **Results:** The activities of α -D-mannosidase isozymes (neutral and intermediate α -D-mannosidase) were significantly high in patients with icteric acute hepatitis (IAH)(48.4 ± 25.4 , 17.6 ± 12.9 , 12.2 ± 6.2), anicteric acute hepatitis (AAH)(29.9 ± 16.0 , 11.9 ± 5.3 , 10.2 ± 3.1), cholestatic hepatitis (ChH) (118.3 ± 20.6 , 50.3 ± 12.2 , 37.0 ± 5.5), icteric liver cirrhosis (ILC)(36.6 ± 13.5 , 12.0 ± 7.8 , 9.6 ± 4.3), ILC with hepatocellular carcinoma (HCC)(39.0 ± 16.5 , 15.1 ± 9.4 , 11.1 ± 5.8). The activity of β -D-mannosidase was also significantly high in patients with IAH (212 ± 36), icteric chronic hepatitis (ICH)(193 ± 25), ACH (196 ± 25), ChH (252 ± 38), ILC (188 ± 21), ILC with HCC (217 ± 55), and ALC with HCC (203 ± 34). **Conclusions:** The activities of α - and β -D-mannosidase were significantly increased in liver diseases with jaundice, which was related to the increased permeability of the liver cell membrane and the leakage of the enzymes into the blood in large quantities. Serial measurement of these enzymes will be helpful to diagnose liver diseases and to understand the clinical conditions of the patients. (Kor J Gastroenterol 1999;33:211 - 221)

Key Words: Liver disease, α - & β -D-Mannosidase

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α -D-mannosidase (α -D-mannosidase monohydrolase,

EC 3.2.1.24) oligosaccharide 가 oligo-
gosaccharide α-D-monnose α-D-mannosidase
13 cytopla-
sam,45 lysosome,5 endoplasmic reticulum6 Golgi 가 가
27 , lysosome α
-D-mannosidase, Golgi α-D-mannosi-
dase cytoplasm endoplasmic reticulum
α-D-mannosidase pH가 4.0-4.6,58
5.5-5.829 6.0-6.54 isozyme
pH가 4.0-4.6 isozyme β-D-mannosidase
acid α-D-mannosidase, pH가 5.5-5.8 isozyme
intermediate α-D-mannosidase, pH가 6.0-6.5
isozyme neutral α-D-mannosidase 9,10 mannositase
가
β-D-mannosidase (β-D-mannoside monohydrolase,
EC 3.2.1.25)
β-D-mannose 가
1,11 lysosome
,11,12
가 13,14
1.
가 가 15 30 , 18

Table 1. Demography of Controls and Patients with Liver Diseases

Diagnosis	Number of cases (Male/Female)	Age (years)(Mean ± SD)
Healthy controls	30 (21/ 9)	37.9 ± 19.0
Acute hepatitis	18 (9/ 9)	39.3 ± 10.8
Icteric	10 (4/ 6)	38.9 ± 11.8
Anicteric	8 (5/ 3)	39.9 ± 5.3
Chronic hepatitis	40 (34/ 6)	35.0 ± 11.9
Icteric	9 (7/ 2)	44.0 ± 8.5
Anicteric	31 (27/ 4)	33.4 ± 11.6
Cholestatic hepatitis	5 (4/ 1)	43.8 ± 17.5
Liver cirrhosis	65 (52/13)	49.9 ± 12.0
Icteric	31 (26/ 5)	49.6 ± 10.3
Anicteric	34 (26/ 8)	50.2 ± 13.5
Liver cirrhosis with HCC	23 (21/ 2)	53.2 ± 10.6
Icteric	16 (16/ 0)	55.3 ± 9.6
Anicteric	7 (5/ 2)	48.4 ± 11.9

HCC, hepatocellular carcinoma.

	5	α -D-Mannosidase	β -D-Mannosidase	213
, 40 , 5 ,	3)			
65 , 23		bilirubin	Abbott EPX	
.			mg/100 μ l	
21 , 9 , 37.9 ,				
9 , 9 , 39.3 ,		ALP, AST ALT	Instru	
34 , 6 , 35 ,		mentation Laboratory Monarch		
4 , 1 , 43.8 ,		IU/liter	.	
52 , 13 , 49.9 ,				
21 , 2 , 53.2	4) α -D- β -D- Mannosidase			
(Table 1).	acid α -D-mannosidase		4-	
	nitrophenyl α -D-mannopyranoside			
	pH 4.5 (0.5 M acetate buffer; pH 4.5), 37			
	10		4-nitrophenol	
	400 nM		Opheim	
, , X- , ,	Touster 5			
.	neutral α -D-mannosidase		4-	
	nitrophenyl α -D-mannopyranoside			
2.	pH 6.2 (0.5 M cacodylate buffer; pH 6.2), 37			
1)	20		4-nitro-	
	phenol 400 nM		Shoup	
5 ml	Touster 4		intermediate α -D-	
30	mannosidase		4-nitrophenyl α -D-	
	mannopyranoside		pH 5.5 (0.5 M	
	acetate buffer; pH 5.5), 37		30	
	4-nitrophenol			
	Tulsiani 7			
2)	1 1 μ l			
4-Nitrophenyl α -D-mannopyranoside, 4-nitrophenyl	4-nitrophenol nmol		.	
β -D-mannopyranoside, 4-nitrophenol, sodium caco-	β -D-mannosidase		4-nitro-	
dylate trihydrate, bovine serum albumin, glycine,	phenyl β -D-mannopyranoside		pH	
cobalt chloride, α -D-mannosidase (from Turbo Cor-	3.5 (0.25 M acetate buffer; pH 3.5), 37			
nuitus; M0893) β -D-mannosidase (from Snail;	1		4-nitrophenol	
M9400) Sigma EPX	Bartholomew Perry 20			
bilirubin Abbott , Monarch	1 1 μ l			
aspartate transaminase (AST), alanine transa-	4-nitrophenel nmol		.	
minase (ALT) alkaline phosphatase (ALP)				
.	5)			
	α -D- β -D-			
	mannosidase	Student t-test	Pearson cor-	

relation

± , 가 가
0.05 가

1. (Table 2)				2. α-D-mannosidase isozyme (Table 3)			
	bilirubin	0.6 ± 0.2,					
ALP	85.3 ± 21.5,	AST	27.1 ± 6.3	1)			
,	ALT	30.7 ± 10.1	.		acid, neutral	interme-	
,		,	,	diate α-D-mannosidase		15.2 ± 6.1	
	bilirubin	8.3 ± 6.2, 9.8		nmol 4-nitrophenol ml-lmin-l(		)	
± 8.9, 5.1 ± 2.6, 7.3 ± 6.6		27.0 ± 13.8		dase	acid α-D-mannosi-	48.4 ±	
	가 가	.		25.4	3.2	가	
,	,			(p<0.01),			
	ALP			29.9 ± 16.0		2	
190.6 ± 66.3, 176.2 ± 99.3, 251.9 ± 131.5		350.4		가	(p<0.05).		
± 114.4				53.3 ± 29.8		3.5	
	가 가			가	(p<0.01),		
	AST	ALT		20.2 ± 8.5			

Table 2. Biochemical Liver Profiles in Controls and Patients with Liver Diseases

Diagnosis	Bilirubin (mg/dL)	ALP (IU/L)	AST (IU/L)	ALT (IU/L)
Healthy controls (n=30)	0.6 ± 0.2	85.3 ± 21.5	27.1 ± 6.3	30.7 ± 10.1
Acute hepatitis (n=18)	5.0 ± 5.8	117.3 ± 30.8	412.5 ± 351.4	767.6 ± 497.4
Icteric (n=10)	8.3 ± 6.2	122.3 ± 33.8	452.8 ± 401.3	821.7 ± 521.3
Anicteric (n=8)	1.0 ± 0.1	111.1 ± 27.4	362.1 ± 296.0	700.0 ± 492.0
Chronic hepatitis (n=40)	3.0 ± 5.5	122.2 ± 62.4	147.2 ± 239.0	292.1 ± 408.0
Icteric (n=9)	9.8 ± 8.9	190.6 ± 66.3	327.6 ± 468.7	639.9 ± 726.9
Anicteric (n=31)	1.0 ± 0.2	102.4 ± 45.7	94.9 ± 55.4	191.1 ± 169.4
Cholestatic hepatitis (n=5)	27.0 ± 13.8	350.4 ± 114.4	130.0 ± 107.7	183.0 ± 97.0
Liver cirrhosis (n=65)	2.9 ± 2.8	144.8 ± 85.6	92.8 ± 96.7	84.9 ± 106.8
Icteric (n=31)	5.1 ± 2.6	176.2 ± 99.3	133.6 ± 123.9	118.0 ± 139.7
Anicteric (n=34)	0.9 ± 0.3	116.2 ± 58.8	55.7 ± 34.7	54.8 ± 49.2
Liver cirrhosis				
with HCC (n=23)	5.3 ± 6.2	230.0 ± 118.1	237.5 ± 268.6	111.7 ± 119.5
Icteric (n=16)	7.3 ± 6.6	251.9 ± 131.5	307.8 ± 297.0	131.0 ± 138.9
Anicteric (n=7)	1.0 ± 0.2	180.1 ± 60.7	76.7 ± 27.5	67.4 ± 28.9

All values are expressed as mean ± SD; Normal references: bilirubin, total <1.0 mg/dL; ALP, 40-170 IU/L; AST, 0-45 IU/L; ALT, 0-45 IU/L; HCC, hepatocellular carcinoma.

Table 3. Activities of Various Serum α -D-Mannosidases in Controls and Patients with Liver Diseases

Diagnosis	Acid α -D-mannosidase	Neutral α -D-mannosidase	Intermediate α -D-mannosidase
Healthy controls (n=30)	15.2 $\pm$ 6.1	6.7 $\pm$ 4.0	5.4 $\pm$ 2.7
Acute hepatitis (n=18)	40.2 $\pm$ 23.1 [*]	15.1 $\pm$ 10.4 †	11.3 $\pm$ 5.1 [*]
Icteric (n=10)	48.4 $\pm$ 25.4 †	17.6 $\pm$ 12.9 [*]	12.1 $\pm$ 6.2 †
Anicteric (n=8)	29.9 $\pm$ 16.0 [*]	11.9 $\pm$ 5.3 †	10.2 $\pm$ 3.1 [*]
Chronic hepatitis (n=40)	27.5 $\pm$ 20.9 [*]	11.9 $\pm$ 10.6 †	9.1 $\pm$ 7.2 †
Icteric (n=9)	53.3 $\pm$ 29.8 †	25.1 $\pm$ 14.1 †	18.1 $\pm$ 9.5 †
Anicteric (n=31)	20.0 $\pm$ 8.5 [*]	8.0 $\pm$ 4.9	6.5 $\pm$ 3.6
Cholestatic hepatitis (n=5)	118.3 $\pm$ 20.6 [*]	50.3 $\pm$ 12.2 †	37.0 $\pm$ 5.5 [*]
Liver cirrhosis (n=65)	29.0 $\pm$ 15.0 [*]	9.5 $\pm$ 6.5 [‡]	8.1 $\pm$ 4.3 †
Icteric (n=31)	36.6 $\pm$ 13.5 [*]	12.0 $\pm$ 7.8 [‡]	9.6 $\pm$ 4.3 [*]
Anicteric (n=34)	22.0 $\pm$ 12.9 †	7.2 $\pm$ 4.0	6.7 $\pm$ 3.9
Liver cirrhosis with HCC (n=23)	32.8 $\pm$ 18.3 [*]	12.2 $\pm$ 9.1 [*]	9.0 $\pm$ 5.9 [*]
Icteric (n=16)	39.0 $\pm$ 16.5 [*]	15.1 $\pm$ 9.4 [‡]	11.1 $\pm$ 5.8 †
Anicteric (n=7)	18.8 $\pm$ 14.8	5.6 $\pm$ 3.2	4.0 $\pm$ 1.7

All values are expressed as mean $\pm$ SD, nmol 4-nitrophenol/ml $\cdot$ min; Significant differences from healthy control(*, $p < 0.05$; †, $p < 0.01$; [‡], $p < 0.001$); HCC, hepatocellular carcinoma.

1.3	가	($p < 0.05$).	18.1 $\pm$ 9.5
	118.3 $\pm$ 20.6		3.4 가 ($p < 0.01$).
7.8	가	($p < 0.001$).	37.0 $\pm$ 5.5
	neutral α -D-mannosidase		6.9 가 ($p < 0.001$).
		가	
		17.6 $\pm$ 2)	
12.9	2.6	가	acid α -D-mannosidase
	($p < 0.05$),		36.6 $\pm$ 13.5
11.9 $\pm$ 5.3	1.8	2.4	가 ($p < 0.001$).
가	($p < 0.01$).		22.0 $\pm$ 12.9
25.1 $\pm$ 14.1	3.8	1.5	가 ($p < 0.01$).
가	($p < 0.01$).		neutral α -D-mannosidase
50.3 $\pm$ 12.2	7.5		12.0 $\pm$ 7.8
가	($p < 0.01$).	1.8	가 ($p < 0.001$).
	intermediate α -D-mannosidase		
		가	
가			intermediate α -D-mannosidase
12.2 $\pm$ 6.2	2.3		9.6 $\pm$ 4.3
가	($p < 0.01$).	1.8	가
10.2 $\pm$ 3.1	1.9	($p < 0.001$).	
가	($p < 0.001$).	가	

Table 4. Activities of Serum β -D-Mannosidase in Controls and Patients with Liver Diseases

Diagnosis	Lysosomal β -D-mannosidase
Healthy controls (n=30)	174 $\pm$ 22
Acute hepatitis (n=18)	203 $\pm$ 36 [‡]
Icteric (n=10)	212 $\pm$ 36 [‡]
Anicteric (n=8)	192 $\pm$ 23
Chronic hepatitis (n=40)	195 $\pm$ 25 [‡]
Icteric (n=9)	193 $\pm$ 25*
Anicteric (n=31)	196 $\pm$ 25 [‡]
Cholestatic hepatitis (n=5)	252 $\pm$ 38 [‡]
Liver cirrhosis (n=65)	187 $\pm$ 24*
Icteric (n=31)	188 $\pm$ 21*
Anicteric (n=34)	186 $\pm$ 27
Liver cirrhosis with HCC (n=23)	213 $\pm$ 49 †
Icteric (n=16)	217 $\pm$ 55 †
Anicteric (n=7)	203 $\pm$ 34 †

All values are expressed as mean $\pm$ SD, nmol 4-nitrophenol/ml $\cdot$ min.; Significant differences from healthy control (*, $p < 0.05$; †, $p < 0.01$; ‡, $p < 0.001$).

3)

acid, neutral intermediate α -D-mannosi-
dase 39.0 $\pm$ 16.5,
15.1 $\pm$ 9.4 11.1 $\pm$ 5.8
2.6 , 2.3 2.1 가
($p < 0.001$, $p < 0.01$ $p < 0.01$).

가 .

3. β -D-
mannosidase (Table 4)

 β -D-mannosidase193 $\pm$ 25 217 $\pm$ 55

1.1 1.3 가

($p < 0.05$, $p < 0.01$), 196 $\pm$ 25 203 $\pm$ 34 1.11.2 가 ($p < 0.001$, $p <$

0.01).				0.58 (p<0.001)	ALT		
				r=0.57 (p<0.001), r=0.45 (p<0.01)		r=0.49	
212 ± 36, 252 ± 38	188 ± 21			(p<0.01)	AST		
1.2 , 1.5	1.1	가		r=0.58 (p<0.001), r=0.50 (p<0.01)		r=0.51	
(p<0.001, p<0.001, p<0.05).				(p<0.001)			
가				3)			
4.	α - D- mannosidase			acid, neutral	intermediate α -D-mannosi-		
isozyme				dase	bilirubin , ALP,		
	(T able 5)			ALT	AST		
				가			
1)				4)			
acid, neutral	intermediate α -D-manno-			acid, neutral	intermediate α -D-mannosi-		
sidase	bilirubin			dase	bilirubin , ALP,		
	(r)			ALT	가		
r=0.73 (p<0.001), r=0.83 (p<0.001)	r=0.57			AST	neutral intermediate α -D-mannosidase		
(p<0.05)							
2)					acid, neutral	intermediate α -D-	
acid, neutral	intermediate α -D-manno-			mannosidase	bilirubin		
sidase	bilirubin , ALP,				r=0.47 (p<0.001), r=0.57 (p<0.001)		
ALT	AST	가		r=0.40 (p<0.001)	ALP		
				r=0.36 (p<0.01), r=0.37 (p<0.01), r=0.40			
acid, neutral	intermediate α -D- manno			(p<0.001) r=0.25 (p<0.05)	neutral		
sidase	bilirubin			intermediate α -D-mannosidase	AST		
r=0.79 (p<0.001), r=0.73 (p<0.001)				r=0.30 (p<0.05)	r=0.25		
r=0.71 (p<0.001)	ALP			(p<0.05)			
r=0.57 (p<0.001), r=0.59 (p<0.001)	r=						

Table 6. Correlation Coefficients between Various Serum β -D-Mannosidases Activities and Biochemical Liver Profiles in Patients with Liver Diseases

Profiles	AH	CH	ChH	LC	HCC
Total bilirubin (mg/dL)	0.43	-0.02	-0.88*	0.007	-0.03
ALP (IU/L)	0.20	-0.07	-0.26	0.21	0.25
AST (IU/L)	0.03	-0.04	-0.60	0.25*	0.28
ALT (IU/L)	0.02	0.05	-0.60	0.07	0.08

*, p<0.05.; AH, acute hepatitis; CH, chronic hepatitis; ChH, cholestatic hepatitis; LC, liver cirrhosis; HCC liver cirrhosis with hepatocellular carcinoma; ALP, alkaline phosphatase; AST, aspartate transaminase; ALT alanine transaminase.

				mannosidase			
5)							
acid, neutral		intermediate		α -D-manno-			
sidase		bilirubin					
		bilirubin		32		4	
		$r=0.60$ ($p<0.01$), $r=0.56$		27		22	
($p<0.01$)		$r=0.54$ ($p<0.01$)		9		α -D- mannosidase	
5.		β - D- mannosi-		가		.18 9	
dase				가		acid intermediate	
		(T able 6)		α -D-mannosidase		가	
		β -D-mannosidase		17		16 10	
bilirubin						acid α -D-mannosidase	
AST							
		β -D-man-		α -D-mannosidase		가	
nosidase		bilirubin		.19		18.64%	
$r=-0.88$ ($p<0.05$)						가	
, AST		$r=0.25$ ($p<0.05$)		α 1-antitrypsin		β -D-	
		α -D-mannosidase		mannosidase		가	
		3 isozyme		22		α	
acid, neutral		intermediate α -D-mannosidase		-D-mannosidase		가	
47-1021		lysosome					
acid α -D-mannosidase		가					
,58							
Golgi intermediate α -D-mannosidase		가					
cytoplasm endoplasmic reticulum		neutral					
α -D-mannosidase		가		가		가	
.4							
endoplasmic reticulum Golgi		α -D-					
mannosidase glycoprotein							
asparagine linked oligosaccharide							
		.23 β -D-		diat α -D-mannosidase		acid, neutral interme	
mannosidase				, acid α -D-mannosidase		가	
lysosome .11-14		α β		가		가	
-D-mannosidase 10,12,19							
9,13,14						β	

-D-mannosidase 가 . acid,
 α -D-man- neutral intermediate α -D-mannosidase .
 nosidase isozyme Zheng Ren18 가
 α -D-mannosidase AST23
 . acid α acid, neutral intermediate α
 -D-mannosidase 가 -D-mannosidase neutral, in-
 Reglero 16 . intermediate α -D-mannosidase β -D-mannosidase
 α -D-mannosidase manno
 가 sidase가 가
 가 , . , α
 man- α
 nosidase -D-mannosidase isozyme ALT AST
 가 가 가 . 가 β -D-mannosi-
 , , , dase ALT ALP 가 ,
 가 ALP
 acid, neutral in-
 intermediate α -D-mannosidase
 mannosidase
 ALT, AST ALP
 가 .
 α -D-mannosidase isozyme β -D-
 mannosidase 가 mannosidase
 가 가
 가 가 .
 가 가
 α -D-mannosidase isozyme
 β -D-mannosidase 가 가 , ,
 15 가 가 mannosidase 가
 가 bilirubin 가
 . 가 , 5
 bilirubin man-
 가 nosidase 가
 , 가 가
 α -D-mannosidase isozyme β .
 -D-mannosidase
 가 가 ALT23

,
 α -D-mannosidase isozyme β -D-
mannosidase가
가 가 ,

,
.

: α -D-mannosi-
dase isozyme β -D-mannosidase
, bilirubin
, ALP, AST ALT

α - β -D-mannosidase
,
: 30 , 18 , 40 ,
5 , 65
23 α - β -D-
mannosidase

Student t-test Pearson correlation
. : ,
, ,

acid, neutral inter-
mediate α -D-mannosidase β -D-mannosidase
48.4, 17.6, 12.2 212, 53.3, 25.1

18.1 193, 118.3, 50.3, 37.0 212, 36.6, 12.0, 9.6
188 39.0, 15.1, 11.1 217
가
가가 가

. acid, neutral intermediate α -D-
mannosidase , ,

bilirubin 가 .
bilirubin, ALP, AST ALT

acid α -D-mannosidase AST
. β

-D-mannosidase

bilirubin
AST . :
 α -D- mannosidase
isozyme β -D-mannosidase가
가 가

: , α - and β -D-mannosidase

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