DISACCHARIDASE DEFICIENCY AND MALABSORPTION OF CARBOHYDRATES

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SYNOPSIS

A large proportion of man's caloric intake is carbohydrate and starch and sucrose account for over three-quarters of the total consumed. But the rapid change of the food industry from an art to a high specialised industry in recent years have made available a variety of rare food sugars, amongst which are various disacharides. Since the digestion or enzymic breakdown of carbohydrates is a normal initial requirement that precedes their absorption, and metabolism of carbohydrates varies according to their molecular structure, these rare sugars can cause diseases of carbohydrate intolerance and malabsorption. Intolerance and malabsorption can be due to polysaccharide intolerance because of amylase dysfunction (caused by the absence of pancreatic amylases) or malfunctioning of absorptive process (caused by damaged or atrophied absorptive mucosa as a result of another primary disease or a variety of other casautive agents or factors, thus resulting in the inability of carbohydrate absorption by the alimentary system). A third type of intolerance is due to primary deficiency or impaired activity of digestive disaccharidases of the small intestine. The physiological significance and the metabolic consequences of such a deficiency or impaired activity of lactase, sucrase-isomaltase, maltase and trehalase are discussed.

INTRODUCTION

Recent years have seen a considerable advance in all facets of enzymology, not least in our understanding of the biochemistry, physiological role, nutritional significance, and industrial potential of the enzymes that hydrolyse disaccharides, the disaccharidases. Understanding of the chemical nature of these enzymes and its relation to catalytic activity has progressed to the point where the enzymes can increasingly be utilised to advantage in food and biotechnology processes, analysis and the diagnosis and treatment of gastrointestinal disorder.

Over the years, with the growth and increased sophistication of the food industry, significant changes have taken place in the types of carbohydrates that are available in our food supplies. Consequently, various rare food sugars are now found in manufactured foods. Since the metabolism of carbohydrates varies according to their molecular structure, disorders of carbohydrate intolerance and malabsorption could arise from the presence of these sugars.

FOOD DISACCHARIDES

Carbohydrates supply a large proportion of man's caloric needs. In the diets of the poor, especially in the tropics they may form as much as 80% of the total calories while in the diets of the rich, the proportion is smaller, but still substantial. Much of this carbohydrate is in the disacharide form, the common ones being sucrose, lactose, and maltose, the breakdown product of starch digestion. These sugars are too large to be absorbed and remains in the small intestine where they are ultimately hydrolysed to their component monosaccharides by the disaccharidases located in the brush border of the mucosal epithelial cells.

Sucrose (α-D-glucopyranosyl β-D-fructofuranoside) is widely distributed in the plant Kingdom and is particularly important in food processing. Lactose or milk-sugar [4-0-(β-D-glucopyranosyl) D-glucose] is a natural constituent of milk, occurring either as the free sugar or in lactose-containing oligosaccharides. Maltose [4-0-(α-D-glucopyranosyl) D-glucose], is not found naturally in abundance in the free state. It is a constituent of the important plant and animal reserve sugars, starch and glycogen. It arises through the hydrolytic action of saliva and pancreatic α-amylase (α-1, 4-glucan 4-glucanohydrolase) on starch. In addition, maltotriose, isomaltose [6-0-(α-D-glucopyranose) D-glucopyranose], and some branched tri-, tetra-, penta- and hexa-saccharides are also produced. A fourth dietary disaccharide is trehalose or mushroom sugar (α-D-glucopyranosyl α-D-glucopyranoside). This naturally occurring non-reducing sugar is a storage sugar of fungi, algae and pteridophytes. In mushrooms and yeasts, it accounts for as much as 15% of dry weight and it can thus be of considerable importance in single cell protein foods.

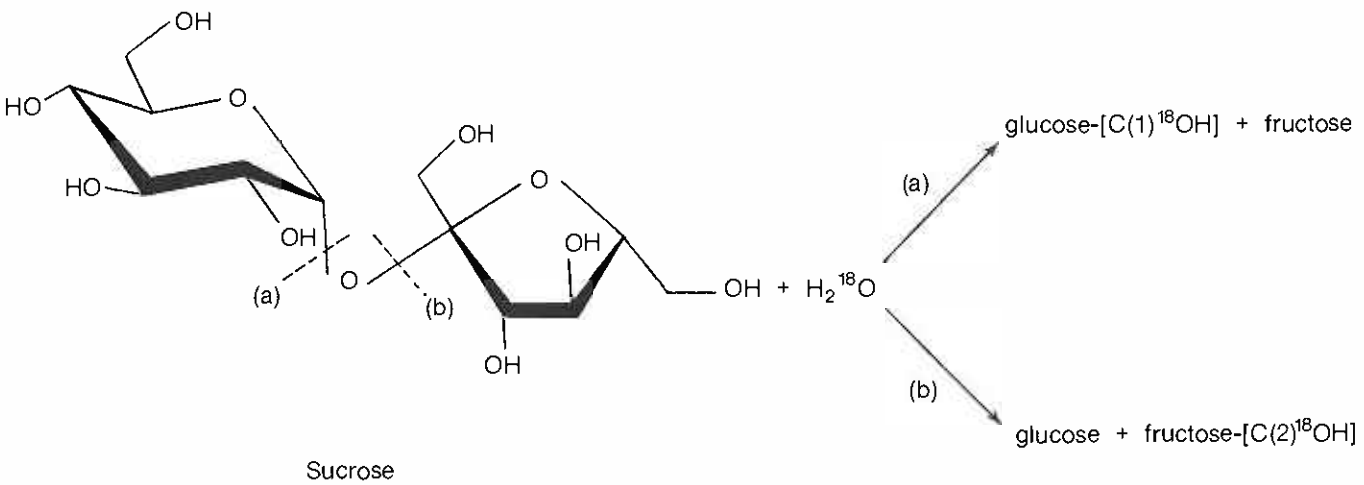
Food disaccharides, and consequently the disaccharidases, the enzymes, that hydrolyse these sugars, have a significant role in food and nutrition (1). The physiological importance of these enzymes is self evident. Disaccharides cannot be utilised as energy sources directly, but must first be hydrolysed to their component monosaccharides prior to absorption. The metabolic consequences of a deficiency or imparied activity of disaccharidases are serious and lead inevitably to clinical symptoms such as diarrhoea, vomiting, abdominal distension and a general failure to thrive (1,2). However, the problem of 'fermentative diarrhoea' received little interest until the later half of the 1950-s when Crane and his coworkers (3) described a completely new model for the events occurring during active transport of certain monosaccharides, thereby focusing interest on sugar digestion and absorption in general.

DISACCHARIDASES

General characteristics

The glycosidic bonds are broken by a hydrolytic mechanism, involving a transfer of components of the substrate to water. The action of carbohydrases generally is highly specific for a particular glycosidic bond linking particular monosaccharides. Thus, sucrose can be cleaved either by an α-glucosidase at position (a) or β-fructofuranosidase at (b) (Fig. 1). The configuration, α or β,

Fig. 1 Mechanism of action of carbohydrases



Sucrose

about the anomeric carbon atom is an important factor in determining whether or not the saccharide will be cleaved by a certain enzyme. For example, both maltose and cellobiose [4-0-(β-D-glucopyranose) D-glucopyranose] are disaccharides composed of two molecules of D-glucose. However, cellobiose possesses a β-glycosidic linkage. Consequently, the two sugars are not cleaved by the same enzyme. The enzymatic hydrolysis of glycosides is essentially reversible, although in most cases the hydrolytic reaction is favoured. However, under suitable conditions, instead of water, the other monosaccharide units present may serve as acceptors and lead to the formation of new disaccharides or even oligosaccharides. The presence of these in significant amounts in foods will undoubtedly lead to metabolic problems.

Disaccharidase activities

Digestion of carbohydrates is initiated in the mouth and stomach by the action of salivary α-amylase. In the small intestine, digestion is continued under the influence of pancreatic α-amylase. All the oligosaccharides are then hydrolysed to the monomeric sugars glucose, galactose and fructose by a group of disaccharidases associated with the brush border membrane (4). The classification of brush border enzyme activities (5) is show in Table 1. The resulting monosaccharides are actively transported by carrier systems (6,7) [although it was generally believed that fructose absorption is not by an active transport system (3)] into the cells and to the portal circulation.

The disaccharidases of the intestinal mucosa hydrolyse α-glucosidic and β-glucosidic linkages. The actual activities of these enzymes are shown in Tables 2 and 3 (8,9). The enzymes are particulate or insoluble enzymes and they are not secreted into the lumen of the small intestine. Apart from trehalase (α, α-trehalose 1-D-glucohyrolase, E.C.3.2.1.28), which hydrolyse only trehalose, the other enzymes have rather broad substrate specificities. These enzymes exist in isoenzyme forms for which the biological significance has not yet been established.

Table 1. Disaccharidases in the brush border of the human intestinal mucosa.

Enzyme or enzyme complex	Substrate	Products
Lactase-glycosylceramidase	Lactose	Glucose Galactose
	Hetero-β-galactoside	Galactose
	Cellobiose	Glucose
	Glycosylceramide	Monosaccharide N-acylspingosine
Sucrase-isomaltase	Sucrose	Glucose Fructose
	Maltose	Glucose
	Palatinose	Glucose Fructose
	α-Dextrins (e.g. isomaltose)	Glucose
Trehalase	Trehalose	Glucose
Two heat stable maltases	Maltose	Glucose
	Isomaltose	Glucose
Glucoamylase (oligosaccharidase)	Malto-oligo-saccharides (2-9 glucose units)	Glucose

Table 2. Disaccharidase activities in jejunal mucosal cells (28).

Subject	Mucosal protein content (mg/g wet weight)	Disaccharidase activity (per g protein)			
		Maltase	Isomaltase	Sucrase	Lactase
Normal subjects					
1	94	500	123	144	39
2	94	502	110	109	89
3	78	1120	268	325	258
4	330	217	56	49	43
5	150	223	65	70	48
6	147	310	122	105	74
7	91	635	216	229	146
8	105	575	164	167	73
9	112	524	122	143	65
10	72	810	172	195	174
11	111	730	225	138	103
12	130	340	87	109	40
Normal subjects with low jejunal lactase activity					
101	86	990	283	255	7
102	103	410	92	115	17
103	112	458	129	139	17
104	91	670	181	188	20
105	130	618	158	234	12
Patients with milk intolerance					
201	176	290	93	107	6
202	103	662	204	220	8
204	132	284	88	74	6

Table 3. Actual activities of disacchardases in normal mucosa (9).

Enzyme	Activity (umol/min/g protein)
Maltase	308.8 + 95.2
Sucrase	101.5 + 30.3
Isomaltase	101.6 + 28.4
Lactase	55.8 + 21.9

ENZYME DEFICIENCY AND MALASSIMILATION OF CARBOHYDRATES

Until recently, very little concrete information has been available about impaired carbohydrate digestion and absorption as a cause of gastrointestinal disease. Most of the evidence on the enzyme defects in disaccharidase deficiency syndromes had been obtained indirectly with blood sugar curves and faecal analysis after oral administration of the sugars. More recently, methods for oral biopsy of the intestinal mucosa had been developed (10).

When intestinal enzyme activity is absent, primary deficiency or enzymopathy is found for lactase (β-D-galactoside galactohydrolase, E.C.3.2.1.23), sucrase, isomaltase, palatinase or trehalase (E.C.3.2.1.28) (Table 4). This malfunction may be fatal if not diagnosed in time. A disaccharide intolerance is classified as primary when it is observed with no history or sign of underlying intestinal disease (Table 4). These defects are inborn errors of metabolism and manifest themselves as isolated defects immediately at birth (as alactasia) or after the introduction of the offending disaccharide into the food (e.g. sucrose). The intestinal mucosa is morphologically normal. These deficiencies persist through life.

Secondary deficiency of disaccharidases is caused by damage to the intestinal mucosa by any of a variety of causative agents or factors, such as viral, bacterial, drugs, malnutrition, etc., leading to secondary intolerance of the disaccharide (Table 4). The intolerance is often transcient. Histologically the changes in intestinal mucosa reflect abnormalities due to the underlying disorder. Hypolactasia is the most frequent disorder.

Since only the liberated monosaccharides can be actively transported by the intestinal cell membrane, a deficiency in or an absence of any disaccharidase activities can result in elevated levels of one or more disaccharides in the colon. These disaccharides (and trisaccharides, tetrasaccharides, etc.) would produce osmotic diarrohoea, causing an increase in the amount of water in the lumen of the colon. The accumulated water causes distension which provokes increased peristalsis and subsequent diarrhoea. Bacterial action in the colon leads to the formation of a variety of products, such as carbon dioxide, hydrogen, lactic acid, acetic acid, ethanol, glycerol and fatty acids. The most frequent symptoms are frothy and explosive watery intermittent diarrhoea, cramps, abdominal distension, audible borborygmi, feeling of bloating, flatulence and possibly nausea and severe abdominal pain.

Lactose intolerance

Approximately 70% of the world's adult population is lactose intolerant (11). It appears that those who have genetically acquired low lactase levels as adults are able to drink milk as infants, but gradually become increasingly lactose intolerant after infancy. We are, however, still unable to explain why a few ethnic groups have developed the ability to retain high intestinal lactase activity throughout life but it is definite that lactase activity is not regulated by adaptation to lactose in the diet of the single individual. Studies (12) have shown that lactase activity is not changed by either lactose or any other sugars; sucrase activity and those of other α-glucosidases, on the other hand, are somewhat increased by certain sugars.

Lactose intolerance is the most widespread and best understood type of carbohydrate intolerance. Primary lactase deficiency (hypolactasia) in adults is not a congenital defect. It is inherited in an autosomal recessive way (13). Lactase activity gradually decreases during growth of the individual to 5-10% of the starting activity. Normally, ingested lactose is hydrolysed by the enzyme lactase, found within the brush border region of the microvilli of the jejunal mucosa, to glucose and galactose, which are then absorbed. If enzyme activity is low, ingested lactose is not hydrolysed. The intact disaccharide is too large to be absorbed and remains in the intestinal lumen. Here it acts osmotically to draw water into the intestine (to dilute the hypertonic load), causing abdominal distension, cramps and increased peristalsis. In addition, the unabsorbed lactose is fermented by certain anaerobic microflora inhabiting the small and

Table 4. The classification of carbohydrate malassimilation

Type	Reduced disaccharidase activity (enzyme deficiency)	Impaired monosaccharide transport (defect in membrane transport)
Primary	Lactase deficiency — congenital absence (alactasia) — adult hypolactasia	Glucose-galactose malabsorption (congenital)
	Sucrase-isomaltase deficiency	
	Trehalase deficiency	
Secondary	Lactase deficiency	Transcient glucose-galactose malabsorption (acquired)
	Lactase deficiency with deficiency of other disaccharidases	

large intestine to lactic acid, which serves as a cathartic. Carbon dioxide and hydrogen are also produced by this fermentation and contributes to the frothy diarrhoea.

A low level of milk consumption is often implicated as the cause of low lactase levels. However, milk drinking does not seem to affect lactase levels although some deficient individuals can gradually increase their milk intake (12,14). On the other hand, prolonged abstinence from lactose in those individuals destined to have high lactase levels does not appear to inhibit lactase activity.

Alactasia, in contrast to hypolactasia, is probably a congenital disease (15) and evidence (16) suggests that this is also an autosomal-recessive trait. It is a condition characterised by the complete absence of lactase in the intestinal mucosa. The consequence of this defect is that lactose is not hydrolysed and all the symptoms of lactose intolerance are present from the first day of life, and persist throughout life. Alactasia is, however, very rare and only about 30 cases have been reported in the literature.

In the absence of lactase, there is also always a lack of glycosylceramidase (phlorizin hydrolase) (Table 1), which constitute the enzyme complex with lactase (17), and this absence probably leads to steatorrhoea which accompanies the lactose intolerance.

Cases of severe infantile gastrogenic lactose intolerance have also been reported (18). This is a very rare disorder and is probably hereditary. It is not caused by any disorder in the disaccharidase activities or by impairment of monosaccharide transport but by abnormal permeability of lactose through the gastric mucosa. Disaccharidas activity in the intestine is normal and, therefore, unlike alactasia, intolerance is not accompanied by diarrhoea (18). The suffering infant vomits excesively and becomes dehydrated (19). Lactosuria and sucrosuria occur followed ultimately by liver damage. The affected child often develops cataracts (18). All symptoms will disappear on a milk-free diet and in some cases milk tolerance may subsequently occur.

Sucrase-isomaltase deficiency

Sucrase-isomaltase deficiency is a rare condition and is in fact a congenital defect in which the enzyme complex consisting of two distinct subunits (20), each acting independently on its specific substrate, is deficient (Table 1). The sucrase-isomaltase complex is composed of a maltase-isomaltase enzyme (E.C. 3.2.1.10) which can hydrolyse maltose, isomaltose, isomaltotriose, isomaltulose, oligo-α-(1,6)-glucosides and oligo-α-(1,4)-glucosides, and a maltase-sucrase (sucrase glucohydrolase, E.C. 3.2.1.48) which can hydrolyse sucrose, maltose, maltotriose and α-(1,4)-glucosides.

The sucrase-isomaltase complex is located chiefly in the jejunum and proximal ileum, being completely absent in the stomach and colon. The activities are greatest in the distal portion of the villi. The sucrase and isomaltase enzymes appear to be subject to the same or very closely related biological control mechanisms. This is clearly indicated by the constancy of the ratio of sucrase to isomaltase activities in random biopsy samples of human intestinal tissue (21) (Table 2), their simultaneous appearance during development (22,23) and their absence from (4) or lack of activity in the brush border region of the intestine of sucrose and isomaltose maldigesters (24).

The mechanism of the hydrolytic action of sucrase and isomaltase (25) involves (i) protonation of the glycosidic oxygen, (ii) splitting of the bond between glycosyl C-1 and glycosidic oxygen, (iii) formation of a carbonium ion which is temporarily stabilised by a carboxylate group present in the enzyme's active site and finally by an OH- from water, with the return of the α-configuration; both sucrase and isomaltase activities lead to retention of configuration.

Sucrase-isomaltase deficiency is an autosomal recessive trait (26), commonly encountered when the sufferer is in early infancy, especially immediately after being weaned, but rarely in adult life. The symptoms of sucrase-isomaltase deficiency appear as soon as foods containing sucrose are introduced into the diet. Deficiency normally manifests itself in young infants as severe diarrhoea resulting in malabsorption syndrome and failure to thrive. In older infants or young children deficiency is indicated by abdominal distension, borborygmi and diarrhoea produced by osmotic effect of unabsorbed oligosaccharides and fermentation products (lactic acid, hydrogen and fatty acids such as butyric acid) within the bowel.

Clinically, sucrose intolerance is more important than isomaltose intolerance. This is simply because, firstly, the amount of isomaltose ingested is always very small since there is only very small amount of isomaltose in the diet, arising mainly from starch and dextrin. Secondly, there are two other intestinal maltases (Table 1) so that intestinal isomaltase activity is never reduced as much as sucrase activity. Thus intolerance of dextrins and starch often disappears in many children in the course of the first year or during the first few years of life and clinical symptoms of starch intolerance are lacking in some patients despite a deficiency of isomaltase activity.

The physiological, biochemical, nutritional and medical aspects of the sucrase-isomaltase enzyme complex was recently reviewed by Cheetham (27).

Maltase defficiency

Congenital maltase deficiency will probably not occur, since in addition to the sucrase and isomaltase (both of which have maltase activity) there are two more maltases (α -1,4-glucan glucanohydrolase, E.C.3.2.1.20) in the mucosa, and these have high enough activities to digest dietary maltose or starch (Table 3).

Trehalase deficiency

Trehalase (α,α -trehalose 1-D-glucohydrase, E.C.3.2.1.28) is a specific enzyme, capable of hydrolysing only trehalose (Table 1). Trehalase deficiency would, therefore, be expected and would manifests itself on ingestion of young mushroom (containing up to 1.4% trehalose) (28,29). The deficiency is however not widely studied and to date only 7 cases have been described in the literature. It is probable that this condition is more common but is no doubt generally considered as intolerant to mushroom.

Trehalose is present in significant quantities in fungi and various other microorganisms. Since some microorganisms are potential protein protein sources for human in the future it is, therefore, not impossible that with changing food habits, trehalase deficiency may become more important than it is at present.

Disaccharidase deficiency and the Eskimos

For a very long time the diet of the Eskimos is essentially free of any carbohydrates. They, therefore, represents a particularly interesting group for study. A recent investigation (30) of the disaccharidase activities of a group of Greenland Eskimos showed, as expected, that nearly all the subjects were lactase deficient (Table 5). The two subjects who had normal lactase activity were closely related to a Dane who had migrated to Greeland and married an Eskimo. Maltase, isomaltase, sucrase and trehalase activities, on the other hand, were normal in most cases. Three of the 19 subjects were, however, practically without sucrase or isomaltase activity while two others had extremely low trehalase activity and three others had moderately low trehalase activity. It thus appears that the 'inborn errors' with absence of one or another of the intestinal disaccharidases, which occur as very rare disease elsewhere, are rather common among the Greenland Eskimos. There is little cause for concern for these enzyme defects among the Eskimos since their diet contains virtually no carbohydrates. However, it is puzzling why these 'mutants' should have become so frequent among the Eskimos.

Table 5. Disaccharidase activities in jejunal biopsies from adult Greenland Eskimos (28).

Subject	Disaccharidase activity (units per g protein)				
	Maltase	Isomaltase	Sucrase	Trehalase	Lactase
Lactose malabsorption					
1	56	16	16	15	1.4
2	226	95	62	10	2.3
3	145	76	61	13	1.7
4	185	67	59	21	1.6
5	334	105	82	8.7	3.0
6	204	86	58	15	2.9
7	43	2.2	0.05	14	1.9
9	319	130	100	42	3.6
10	92	1.5	0.6	20	4.0
11	132	41	29	17	1.5
12	240	82	67	7.7	2.3
13	154	55	46	2.7	8.2
14	159	69	54	6.0	2.0
16	56	1.4	0.02	28	4.3
17	180	59	64	11	2.4
18	192	67	56	9.1	2.1
19	307	82	59	6.0	3.8
No lactose malabsorption					
8	290	105	75	1.5	21
15	236	69	60	14	21

REFERENCE:

1. Lee CK, Lindley MG, eds. Developments in Food Carbohydrates. 111. Disaccharidases. London: Applied Science Publishers, 1982.
2. Dahlqvist A. Enzyme deficiency and malabsorption of carbohydrates. In: Supple HL, McNutt, KW, eds. Sugars in Nutrition. New York: Academic Press, 1974: 187-214.
3. Crane RK: Internal absorption of sugars. Physiol Rev 1960; 40: 789-825. Wilson TH. Intestinal Absorption. Piladalphia: Saunders, 1962.
4. Crane RK, Malathi P, Preiser H: A digestive-absorptive surface as illustrated by the intestinal cell brush border. Trans Amer Microsoc Soc 1975; 94: 529-44.
5. Gray GM. The physiology of intestinal absorption of sugar. In: Jeanes A, Hodge J, eds. Physiological Effects of Food Carbohydrates. Washington: ACS Symposium Series, American Chemical Society, 1975: 181-90.
6. Lutkic A, Votava A. Enzymic deficiency and malabsorption of food disaccharides. In: Lee CK, Lindley, MG, eds. Developments in Food Carbohydrates. 111. Disaccharidases. London: Applied Science Publishers, 1982: 183-211.
7. Gracey M, Burke U, Oshin A: Intestinal transport of fructose. Lancet 1970; 2: 1627-8.
8. Haemmerli UP, Kistler H, Ammann R, et al: Acquired milk intolerance in the adult caused by lactose malabsorption due to a selective deficiency of intestinal lactase activity. Amer J Med 1965; 38: 7-30.
9. Lucking T, Wenner J: Activities of intestinal disaccharidases and alkaline phosphates in jujunal biopsy in children. Eur J Paediat 1976; 121: 263-77.
10. Dahlqvist A: Assay of intestinal disaccharidases. Anal Biochem 1964; 7: 18-25. Methods of assay of intestinal disaccharidases. Anal Biochem 1968; 22: 99-107.
11. Bayless TM, Paige DM, Ferry GD: Lactose intolerance and milk drinking habits. Gastroenterology 1969; 60: 605-8.
12. Rosenwig NS, Herman RH: Diet and disaccharidases. Amer J Clin Nutri 1969; 22: 99-102.
13. Dahlqvist A: The basic aspects of the chemical background of lactase deficiency. Postgrad Med J 1977; 53(suppl. 2-4); 57-62.
14. Keusch GT, Troncale FT, Miller FG, Promadhat V, Anderson PR: Acquired lactose malabsorption in Thai children. Paediat 1969; 43: 540-5.
15. Holzel A, Schwaz V, Sutcliffe KW: Defective lactose absorption causing malnutrition in infancy. Lancet 1959; 1: 1126-8.
16. Newcomer AD, Gordon H, Thomas PJ, McGill DB: Family studies of lactose deficiency in the American Indian: Gastroenterology 1977; 73: 985-8.
17. Cousineau J, Green JR: Brush border membrane lactase. Purification and Kinetic analysis of 3 forms of the enzymes from the proximal and distal small intestine of suckling rats. Biochem Soc Trans 1979; 7: 961-962. Isolation and characterisation of the proximal and distal forms of lactase phlorizin hydrolyase from the intestine of the suckling rats. Biochim Biophys Acta 1980; 615: 147-57.
18. Hirashima Y, Shinozuka S, Ieiri T, Matsuda, I, Ono, Y, Murata, T: Lactose intolerance associated with cataracts. Eur J Paediat 1979; 130: 41-45. Hoskova A, Sabacky J, Mrskos A, Pospisil R: Severe lactose intolerance with lactosuria and vomiting. Arch Dis Child 1980; 55: 304-16.
19. Berg NO, Dahlqvist A, Lindberg T: A boy with severe infantile gastrogen lactose intolerance and acquired lactase deficiency. Acta Paediat Scand 1979; 68: 751-8.
20. Asp N-G, Dahlqvist A: Separation of human intestine sucrase from isomaltase. FEBS Letters 1973; 35: 303-5.
21. Auricchio S, Dahlqvist A, Murset G, Prader A: Isomaltose intolerance casuing decreased ability to utilise dietary starch. J Paediat 1963; 62: 165-7.
22. Rubino A, Zimbalatti F, Auricchio S: Intestinal disaccharidase activities in adult and suckling rats. Biochem. Biophys Acta 1964; 92: 305-11.
23. Dahlqvist A, Lindberg T: Development of the intestinal disaccharidase and alkaline phosphatase activities in the human foetus. Clin Sci 1966; 30: 517-28.
24. Dubs R, Steinmann B Gitzelmann R: Demonstration of inactive enzyme antigen in sucrase-isomaltase deficiency. Helv Paediat Acta 1973; 28: 187-98.
25. Walsh C. Enzyme reaction mechanism. San Francisco: W.H. Freeman 1979.
26. Kerry KR, Townley RR: Genetic aspects of intestinal sucrase-isomaltase deficiency. Aust Paediat J 1965; 1: 223-35.
27. Cheetham PJ. The human sucrase-isomaltase complex: Physiological, biochemical, nutritional and medical aspects. In: Lee CK, Lindley, MG, eds. Developments in Food Carbohydrates. 111. Disaccharidases. London: Applied Science Publishers, 1982: 107-139.
28. Bergoz R: Trehalose malabsorption causing intolerance to mushroom. Gastroenterology 1971; 60: 909-12.
29. Madzarovova-Nohejlova J: Trehalose deficiency in a family. Gastroenterology 1973; 65: 13-33.
30. Asp N-G, Cook GC Dahlqvist A: Activities of brush border lactase, acid β-galactosidase and hetero-β-galactosidase in the intestine of the intestine of lactose intolerant Zambian African. Gastroenterolgy 1973; 64: 405-18.