JEJUNAL DISACCHARIDASE ACTIVITY IN GASTROINTESTINAL BILHARZIASIS

THESIS

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BY

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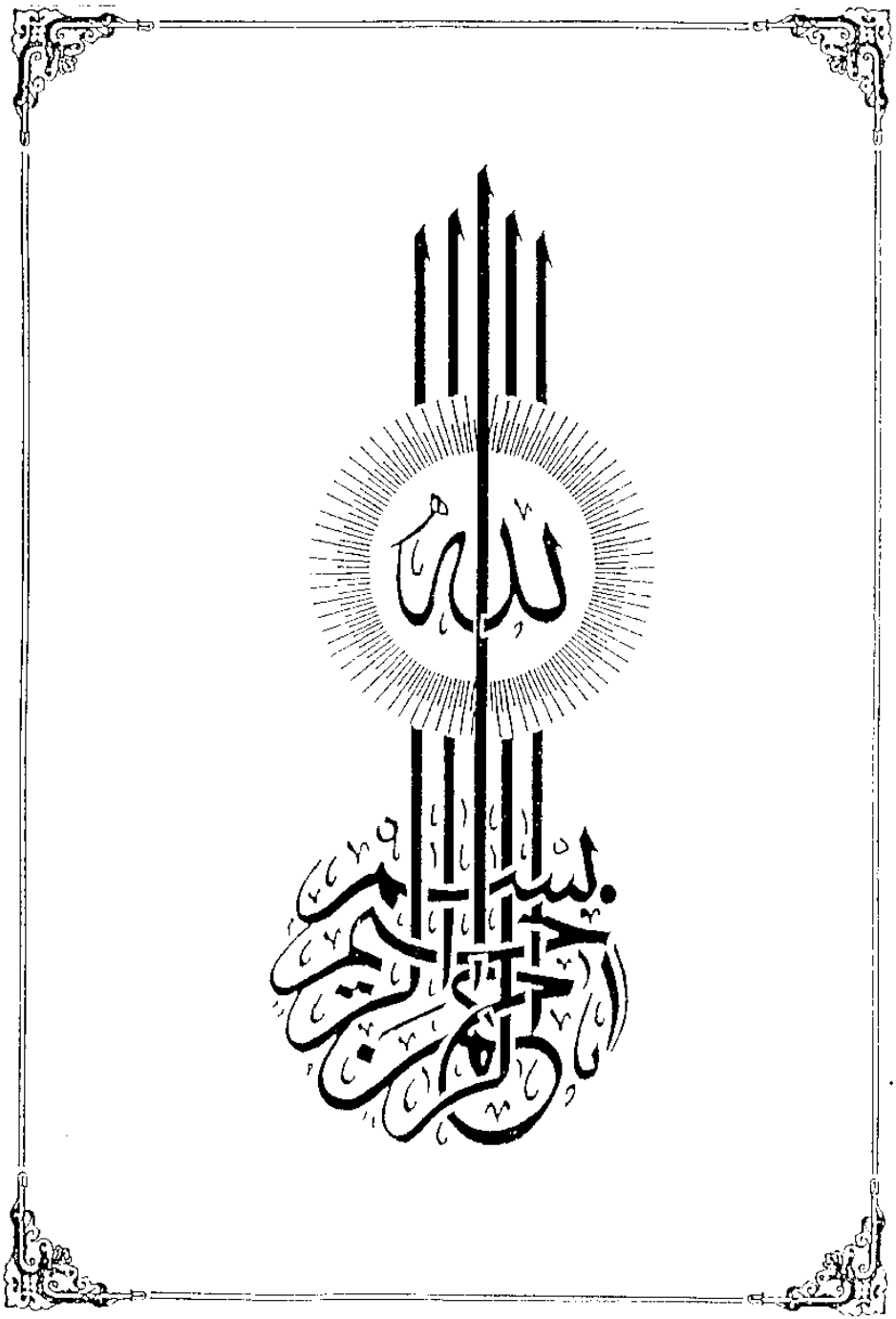

CONTENTS

GENERAL INTRODUCTION AND AIM OF THE WORK

The activities of intestinal disaccharidases in health and various diseases are gaining much interest. In gastrointestinal bilharziases no similar studies have been yet reported. In our countary carbohydrates form the main bulk of diet among the majority of population and also bilharziasis is a general problem, so it seems worthy to study the jejunal disaccharidase activities in gastrointestinal bilharziasis.

The Disaccharidases

Definition

Intestinal disaccharidases are concerned with the hydrolysis of disaccharides to their constituent monosaccharides.

There are varieties of these enzymes acting on different substances. The physiologically important disaccharides are maltose, sucrose, and lactose.(1)

Localisation of disaccharide hydrolysis.

In 1957 Borgstrom and Dahlqvist(2) localised the hydrolysis of disaccharides to the intracellular portion of the gastrointestinal tract.

The brush border membrane of the epithelial cell of hamster small bowel had been isolated by tissue fractionation.(3) The disacchoridase activities were recovered in high yields in these brush border preparations. Electron microscopy of isolated brush borders from epithelial cells of hamster intestine demonstrated knobs, 60A° attached to the lumen suface of the plasma membrane.(4) Separation of these knobs

were done and the activities of sucrase and maltase were shown to reside in these knobs and were not found with the plasma membrane.

Jos et al. 1967[5] demonstrated by a histochemical technique intense staining in the brush border and in the distal part of the villi.

Spatial distribution of disacchardiases:

In the gastric mucosa little disacchardiase activity was found.[6]

In the small bowel the lowest disacchardiase activity was found in the duodenum and distal ileum. In the jejunum and proximal ileum peak activities are found at variable points.[7]

Dietary regulation of disaccharidase activities:

Rosenweig and Hermon in 1968[8] found that normal jejunal sucrase and maltase activites adapt to dietary sugar. Both increased significantly with either sucrose or fructose feeding which has no effect on lactase activity.

Other studies in human [9] [10] [11] have shown that lactose or milk feeding did not increase lactase activity. Also lactose free died did not decrease lactase activity.[12]

In experiments on rat[13] protein free diet did not lower disaccharidase activity.

With the use of radioisotopic assay lactase purified from human intestinal mucosa was inhibited by glucose, galactose and fructose.[14] [15] Sucrase and maltase were inhibited by hydrolytic products of their natural substrates. This inhibition is maximal at pH6. [16] It is probable that inhibition is by competetion for transport by product of hydrolysis which thus a cummulate at site adjacent to the brush border with further inhibition of enzyme activity.[15] Wether this inhibition actually occurs during the course of digesting a meal or can only be produced by ingesting larage amount of monosaccharides is still unclear[15]

Development of intestinal disacchardiases:

All of the intestinal disaccharidases are already active in three month old human embryo.[17] [18] The

alpha disaccharidase activities reach the normal adult level in the 6th and 7th month of foetal life. The only exception is one of the maltases which is still low in the newlyborn.(17) In adults the lactase values are occassionly reduced but still sufficient for hydrolysis of normal lactose intake.(19) In studies on human population with high incience of lactase deficiency.(20) It was found that lactase levels have decreased following the weaning period and the adult levels were usually reached by 10 years of age.

The clinical syndromes based on disaccharidases deficit.

If one or more of disaccharidase enzymes are deficient the corresponding disaccharides are not hydrolysed and remain in the intestinal lumen.(21) The undigested disaccharides are excreted unchanged in foeces causing osmotic diarrhoea. They also undergo bacterial degredation causing fermentative diarrhoea. Therefore diarrhoea is the leading symptom of disaccharide malabsorption.(22) (23) The degree of diarrhoea depends on the dose of the sugar. The abdomen is distended and usually vaguely painful. The distension is due at first to liquid in the small bowel and later to gas in the colon as the sugar reaches the bacteria. Borborygmi are prominent. The stools are liquid, foamy and have typical acid smell.This is due to the presence of lactic acid which is produced by the action of bacteria on undigested disaccharides. It can be determined by chemical methods.(24) Only trace amount is found in normal foeces but big amount is found in formentative diarrhoea.

Lactase deficiency:

In adult the clinical features of lactase deficiency are extremely variable. (25) There may be nausoea,

fullness, abdominal cramps, flatulance and diarrhoea following ingestion of milk or lactose. In some patients the symptoms are very mild or even abscent and in others they are severe.

The factors that determine the symptomatology of lactase deficiency are:[26]

1. The amount of milk or lactose ingested.
2. The total lactase avilable for hydrolysis which is in part a function of the whole length of the small bowel.
3. The speed of gastric emptying.
4. The presence of other foodstaffs.
5. The type of intestinal flora.

When lactase deficit was first described, it was thought to be a residual effect of some illdefined transient injury or inflammation of the gastrointestinal tract.[27] As it was observed that lactase defeciency occurs more frequently with the advance of age, it was suggested that adult lactase deficit might represent late onset of heridietary trait or an effect of aging.[27]

Lactase deficiency was demonstrated in many ethinic groups. This was demonstrated in Asian.[28] [29] North and south American Indians [30] [31], Eskimos[32] Greek cypriots[33] and Egyptians[34] [35] [36] Causcasion maintain relatively high lactase activity throughout adult life.[26]

Evidence of familial basis for primary adult lactose intolerence is found in some studies.[33] [37]

Cook and Kajubi in 1966[38] and Gudmand and Jarnum in 1969[32] studied individuals or groups of mixed percentage whose parents or parent groups have high incidence of lactose intolerance on one hand and low incidence on the other. It hase been found that these mixed individuals have incidence of intolerance intermediate between their parents or parent groups. All these findings suggest that adult lactase deficit is a genetic trait.

It was suggested that lactase deficit in man may be the result of lactose poor diet[39] pointing out to the fact that there is little or no milk consumption in areas where lactase deficiency is prevelant.

However it is equally appropriate to conclude that there is abostenation from milk ingestion because of lactase defeciency.[40]

Combined sucrase isomaltase deficiency is an uncommon heritable disorder which has been noted mostly among children[41] [42] and only in few adults[43][44] As long as the newborn infant is fed human milk, there are no symptoms. When the ingested food contains sucrose, dextrins or starch, diarrhoea appears and the child stops gaining weight and fails to thrive.

The elimination of sucrose, dextrins and starch from diet is followed by quick improvement.

Congenital glucose galactose malabsorption:

Very few cases were reported by Andqvist and Meeuwisse in 1962.[45] As glucose is the constituent. monosaccharide of all disaccharides, all disaccharides tolerance test are abnormal. The only tolerated suger is fructose.

Symptomatic or secondary syndromes:

Any disease with diffuse damage of the small bowel mucosa also damages small intestinal disaccharidases.[46][47]

Patients with primary malabsorption syndromes shows decreased activity of intestinal disaccharidase, and the activity of the enzymes increase after successful treatment with healing of the intestinal epithelium.[6][47][48]

However lactase activity returns slowly to normal within months but sometimes remains severely depressed for years.[47] [49]

The younger the age of the patient the greater the rate of recovery of lactase activity.[47]

Patients with untreated pernicious anaemina shows decreased activity of intestinal disaccharidases.[50][51]

Plotking and Isselbacher 1964[52] reported decreased intestinal disaccharidases with intestinal lymphangiectasia, abetalipoproteinemia and blind loop syndrome.

In 1965 Larrechea et al [53] reported decreased disaccharidase activity with Whipple's disease and intestinal lymphangiectasia.

Neomycin [54] induces a decrease in the activity of intestinal disaccharidases.

Resection of at least 2/3 of the small bowel decreases the total content of disaccharidases and results in disaccharide malabsorption despite normal enzyme concentration in the remaining small bowel.

Chance combination of acquired lactase defeciency with other gastrointestinal diseases:
A chance combination of lactase defeciency with any other disease is expected to be rather frequent. On possible reason is the increase in dietary load of lactose due to the regimens prescribed by physicians for the treatment of some gastrointestinal disorders.[49]