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Suspending Agents in Medicaments as Possible Sources of Galactose to Galactosaemic Child

The need to exclude galactose from the diet of galactosaemic patients is well understood, and the difficulties of achieving this have been well documented. As little as 250 mg. lactose administered daily as a tablet excipient to a galactosaemic child has been reported sufficient to arrest weight gain (Bower and Smallpeice, 1955).

Tragacanth and acacia (gum arabic) are widely used as suspending agents in pharmaceutical liquid preparations; for example several of the BPC or

NF oral suspensions, and sulphadimidine paediatric mixture BNF. Both these gums, as well as carrageenan (Irish Moss) and agar, are used extensively in the food industry. All four are complex galactosides, and therefore potential sources of galactose. A galactosaemic child prescribed two suspensions concurrently for 6-hourly administration would receive 40 ml. of mixture equivalent to 500 mg. gum daily, in addition to intake from foods and confectionery products.

The purpose of our investigation was to find whether these compounds may be hydrolysed *in vivo* to free galactose.

Experimental Work

The concentrations of tragacanth, acacia, agar, and carrageenan used in the following experiments were those normally found in liquid pharmaceuticals and foods. In each experiment, products of hydrolysis were demonstrated by thin-layer chromatography.

(1) Each gum was heated with strong acid at 100 °C. for 4 hours. Products of hydrolysis were demonstrated on Silica Gel G absorbent using chloroform/acetic acid/water (6/7/1) as solvent and α -naphthol/sulphuric acid for visualization.

(2) Each material was incubated at 37 °C. with crude malt diastase (α - and β -amylase) for 2 hours.

(3) A solution of each gum was incubated with human salivary amylase together with a jejunal biopsy specimen of proven normal lactase activity. Each solution was adjusted to pH 6.5 in the presence of chloride ions (0.1%), and incubated at 37 °C. Controls of starch for α -amylase activity, and lactose for lactase activity were incubated to confirm suitable conditions for enzymic digestion.

(4) Solutions, and controls as above, were incubated with hog pancreatic α -amylase and human disaccharidase. Each tube was adjusted to pH 6.5, and incubated at 37 °C.

Several chromatographic systems were examined, and optimum separation was found with cellulose MN 300 as adsorbent 250 μ thick, and ethyl acetate/pyridine/water (2/1/2) as solvent. Using aniline phthalate for visualization, 0.5 μ g. galactose could be detected. This procedure was used in all experiments except (1).

Results

The results are shown in the Table.

It will be noted that free galactose was identified after strong acid treatment, and after digestion with β -amylase. This enzyme is not present in mammalian tissue but commonly occurs in plants and bacteria. Results from incubation with saliva and jejunal enzyme failed to demonstrate galactose after 24 hours, though both controls gave positive results when tested after 1 hour. Similarly, analysis of samples treated for 24 hours with

TABLE

Gum	Result of Hydrolysis			
	Experiment 1 Mineral Acid at 100 °C. for 4 hours	Experiment 2 Crude Malt Diastase (α - and β -amylase) at 37 °C. for 2 hours	Experiment 3 Hog Pancreatic Amylase + Human Disaccharidase at 37 °C. for 24 hours	Experiment 4 Human Salivary Amylase + Human Disaccharidase at 37 °C. for 24 hours
Acacia	Galactose present	Approximately 1% gum hydrolysed to galactose	No galactose found	No galactose found
Tragacanth	Galactose present	Approximately 1% gum hydrolysed to galactose	No galactose found	No galactose found
Carrageenan	Galactose present	Approximately 1% gum hydrolysed to galactose	No galactose found	No galactose found
Agar	Galactose present	Approximately 1% gum hydrolysed to galactose	No galactose found	No galactose found

hog α -amylase and human disaccharidases failed to show free galactose.

Discussion

Though the component sugars in these gums are known, the nature of all the bonds remains to be finalized. The galactose content of the substances varies, but in the case of agar and carrageenan, it is the predominant sugar. Even so, the experiments indicate that these compounds are not attacked by digestive juices in any part of the gastro-intestinal tract. It is relevant that *in vivo* studies have shown that the α -galactosides present in soya bean are resistant to digestion in the intestine, but at the same time are susceptible to bacterial fermentation in the lower sections of the intestinal tract (Gitzelmann and Auricchio, 1965). However, these authors have shown that galactose absorption in this region is extremely limited, and it appears, therefore, that these gums, like the soya galactosides, would also be safe in this respect. One possible exception might exist during gastro-enteritis when bacteria colonize the upper areas of the small intestine where absorption is more rapid.

Conclusion

Tragacanth, acacia, agar, and carrageenan are unlikely to release free galactose for absorption in the gastro-intestinal tract, and may, therefore, be safely included in medicaments for patients suffer-

ing from galactosaemia. Withdrawal of these gums might be advisable during prolonged gastro-enteritis.

Summary

Tragacanth, acacia, agar, and carrageenan are complex galactosides widely used in the preparation of liquid medicaments, foods, and confectionery products. They are a potential source of galactose and may be contraindicated in the galactosaemic child. However, treatment of these agents with α -amylase and human disaccharidases followed by thin-layer chromatographic examination of the hydrolysates failed to show the presence of free galactose. Thus, with the possible exception of patients with gastro-enteritis, when bacterial degradation may hydrolyse the gums in the small intestine where absorption occurs, the use of these gums in medicaments for the galactosaemic child seems safe.

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