XYLITOL: A SUGAR SUBSTITUTE FOR PATIENTS OF DIABETES MELLITUS

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ABSTRACT

India figures conspicuously around the world for rapid growing of diabetes at a high rate and every fifth diabetic in the world is found to be Indian. India is also termed as ‘Diabetic capital of world’ with high prevalence of disease among South Indian population. Obesity, food insecurity, illiteracy, poor sanitation, poor glycemic control and dominance of communicable diseases are the main factors responsible for developing this disease at a fast rate among Indian people. The treatment approaches currently used against diabetes are use of oral drugs, amylin agonists, glucagon antagonists, protein tyrosine phosphatase inhibitors, salicylate derivatives and G protein coupled receptors. The currently used therapeutic approaches against diabetes are costly and resulting in various side effects like allergic reactions, swollen ankles, weight gain, abdominal pain and digestive disturbances. The use of natural alcoholic sugars like sorbitol, mannitol, xylitol, erythritol, maltitol and lactitol is another alternative treatment against diabetes for controlling sugar levels. Among various alcoholic sugars, xylitol is found to be most effective due to its unique properties, resulting in its wide use in many industrial applications. In addition, GRAS status has been given to xylitol by FDA, USA in 1986 and is approved to be safe for human consumption. Currently, most of the xylitol demand has been met by its chemical synthesis, which is costly and resulting in low product yield. The alternative approach for synthesis of xylitol is biotechnological methods using whole cells and enzymatic methods by utilizing various low cost agricultural wastes as raw materials to decrease its production cost and increasing product yield. The Government of India should
also need to focus on planning some projects on utilization of these agricultural wastes, which are produced in huge amounts annually in India, for xylitol production to fulfill the need of xylitol for Indian market.

**KEYWORDS**: Xylitol, Xylose, Diabetes, Xylitol, Agricultural waste, Sweetener, Alcoholic sugar.

**INTRODUCTION**

Diabetes is a rapidly growing non communicable disease in India with prevalence of 69.2 million and it is rising day by day at a high rate.\(^1\) This disease is found to be more prevalent among the population of urban areas compared to rural one. Various studies indicate the high prevalence of diabetes among people of South Indians than North Indians.\(^2\) Obesity, food insecurity, illiteracy, poor sanitation, poor glycemic control and dominance of communicable diseases are the main factors responsible for this disease.\(^3-4\) Currently, various therapeutic approaches are available to control diabetes, however, these treatments are not cost effective and associated with many side effects. The use of natural alcoholic sugars like sorbitol, mannitol, xylitol, erythritol, maltitol and lactitol is another alternative strategy against diabetes for controlling sugar levels. Amongst various alcoholic sugars, xylitol is found to be most effective due to its unique properties like sweetening power similar to sucrose, its metabolism independent to insulin, absence of maillard reaction, negative heat of dissolution, anticariogenicity and antiketogenicity. The current paper summarizes the magnitude of diabetes in India, need to control diabetes, treatments available for this disease, use of xylitol as sugar substitute for diabetic patients, processes for xylitol production, global status and safety issues of xylitol.

**MAGNITUDE OF DIABETES: INDIAN SCENARIO**

Diabetes is growing rapidly at an alarming rate in India and that is why India is being termed as ‘diabetes capital of world’.\(^5\) Currently, the prevalence of this major non communicable disease (NCD) in India is 69.2 million, which is expected to be rise at a rate of 78.5% (123.5 million) by the year 2040. From the world record with diabetic patients, every fifth diabetic in the world is found to be an Indian.\(^1\) The Atlas of Diabetes (2006) published by International Diabetes Federation revealed the urgent need to follow the preventive steps against this rapidly rising disease.\(^5\) The incidence of diabetes varies with the geographical distribution with one quarter in rural populations that of urban populations.\(^2\) The first national study on prevalence of diabetes was done between 1972 and 1975 by Indian Council of
Medical Research (ICMR) and this disease was found to be highly prevalent in urban population compared to rural population. Previous studies conducted by Indian Council of Medical Research (ICMR) proved the lower prevalence of this disease in population of North India like Chandigarh, 0.12 million and Jharkhand, 0.96 million compared to other states like Maharashtra, 9.2 million and Tamil Nadu, 4.8 million. Similar trend of diabetes were recorded in metropolitan cities located in different directions of India like Kolkata, 11.7%; Kashmir Valley, 6.1%; New Delhi, 11.6%; Mumbai, 9.3%; South India: Chennai, 13.5%; Hyderabad, 16.6% and Bangalore, 12.4% by National Urban Diabetes Survey.

NEED TO CONTROL DIABETES
The major concern of rising diabetes was also noticed by the Government of India due to rapid increase of this deadly disease, which has reached at epidemic range in some parts of the country. This epidemic disease results in loss of national productivity and exchequer at social level. There is an immediate need to generate awareness among people for early detection, cost effective management and rehabilitation of diabetic patients. The major factors responsible for this disease are obesity, food insecurity, illiteracy, poor sanitation, poor glycemic control and dominance of communicable diseases. It is clear from the world record that diabetes is very prevalent among the people of India and thus it has become important to control the spread of this disease at a large scale. Many previous studies on diabetes also suggested the need for developing government policies, interventions and public awareness programmed in India to overcome the spread of this disease in the future generation.

TREATMENTS AVAILABLE TO CONTROL DIABETES
Several oral drugs like biguanides, sulfonylureas, glinides, thiazolidinediones, amylin agonists, glucagon antagonists, protein tyrosine phosphatase inhibitors, salicylate derivatives and G protein coupled receptors are used to treat diabetes. However, these treatments are costly and associated with many side effects like allergic reactions, swollen ankles, weight gain, abdominal pain and digestive disturbances. Several non-nutritive, high intensity sugar alcohols like sorbitol, mannitol, xylitol, erythritol, maltitol and lactitol are available in the market for diabetic people due to their low calorie value, low glycemic index with high rate of controlling blood sugar levels. The relative sweetness and nutritive value of various polyol sugars is given in Table 1.
Table 1: Relative sweetness and nutritive value of various polyol sugars.

<table>
<thead>
<tr>
<th>Sugar Alcohol</th>
<th>Relative sweetness (Sucrose=1)</th>
<th>Nutritive value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xylitol</td>
<td>1.0</td>
<td>2.4</td>
</tr>
<tr>
<td>Lactitol</td>
<td>0.4</td>
<td>2.0</td>
</tr>
<tr>
<td>Sorbitol</td>
<td>0.6</td>
<td>2.6</td>
</tr>
<tr>
<td>Erythritol</td>
<td>0.7</td>
<td>0.2</td>
</tr>
<tr>
<td>Mannitol</td>
<td>0.5</td>
<td>1.6</td>
</tr>
<tr>
<td>Maltitol</td>
<td>0.9</td>
<td>2.1</td>
</tr>
<tr>
<td>Isomalt</td>
<td>0.5</td>
<td>2.0</td>
</tr>
<tr>
<td>Hydrogenated starch hydrolysates</td>
<td>0.3</td>
<td>3.0</td>
</tr>
</tbody>
</table>

**XYLITOL AS SUGAR SUBSTITUTE FOR DIABETIC PATIENTS**

Xylitol is pentitol sugar (C₅H₁₂O₅) with sweetening power similar to sucrose but with low calorie content. This alcoholic pentose sugar is found naturally in many fruits and vegetables like yellow plum, strawberries, raspberries, cauliflower and lettuce. The glycemic index of xylitol is low because it is not actively transported through intestinal tract. The high tolerance of xylitol by diabetics is due to its metabolism in humans by two different pathways, such as direct absorption (mainly in liver) and indirect metabolism by intestinal bacteria. Both of these mechanisms of xylitol metabolism are independent to insulin and hence it acts as promising ideal alternate sweetner for diabetics. Xylitol controls blood glucose, lipid level and weight control, which are the three important objectives for diabetes management. It is poorly absorbed by the human digestive system and thus acts as a dietary soluble fiber to maintain healthy gut flora. Xylitol acts as prebiotic and fermented by the bacteria of large intestine into low calories short chain fatty acids. These fatty acids are absorbed by small intestine into blood circulation where they act as source of energy for various metabolic pathways. Hence, this polyol sugar is very good supplement as sugar for diabetic patients.

**PROCESSES FOR PRODUCTION OF XYLITOL**

There are mainly three processes for the production of xylitol such as solid liquid extraction, chemical synthesis and biotechnological methods. Currently, the industrial demand of xylitol has been met through its synthesis by chemical hydrogenation of xylose at high temperature and pressure in the presence of catalyst. However, there are many limitations associated with this chemical process like high process cost, low product yield and hazardous effects on environment. In the process of solid liquid extraction, xylitol is recovered from the natural sources (fruits and vegetables), but small percentage present in natural sources is major hindrance to make this process economical. Biotechnological methods are based on
utilization of microorganisms or purified enzyme for the production of xylitol by utilizing various agricultural lignocellulosic waste materials derived from wood, grass, forestry waste, agricultural residues and municipal solid wastes are center of attraction for researchers now a days.\textsuperscript{[19]} Candida guilliermondii and Candida tropicalis are two commonly used yeasts for the production of high yield of xylitol.\textsuperscript{[20-21]} Most of the previous research on production of xylitol using biotechnological methods has been conducted with whole microbial cells (mainly yeasts) and recombinant organisms and very little work has been reported with purified xylose reductase enzyme. Hence, researchers should focus on enzymatic production involving recent techniques like protein engineering using bioinformatics tools needs to be done for economical production of xylitol.

GLOBAL STATUS FOR USE OF XYLITOL
The global market of xylitol is increasing day by day and it is estimated to be USD 1 billion by 2020.\textsuperscript{[22]} In addition to substituent as sugar, there are various potential applications of xylitol in different industrial sectors, such as food, pharmaceutical, odontological, cosmetics and textiles.\textsuperscript{[23-27]} The wide applications of xylitol are due to its unique properties like sweetening power similar to sucrose, its metabolism independent to insulin, absence of maillard reaction, negative heat of dissolution, anticariogenicity and antiketogenicity. The products of xylitol available in the market are Epic-xylitol gums, B-FRESH gums, Tic Tac “Silvers”, Xylitol (100% pure natural sweetener), Omnii “Theramints”.\textsuperscript{[28]} The major xylitol market share is dominated by chewing gums applications followed by confectionery and food sectors. However, a small amount of xylitol is used in the pharmaceuticals and nutraceuticals.\textsuperscript{[29]} Moreover, most of the xylitol products have been manufactured by USA and its demand in India is catered through imports. Therefore, there is an utmost need to focus on biotechnological production of xylitol by utilizing various lignocellulosic waste as raw materials. The Government of India should need to focus on planning some projects on economical xylitol production to fulfill the need of xylitol for Indian market by involving biological methods.

SAFETY ISSUES OF XYLITOL FOR DIABETICS
GRAS (Generally Recognized as Safe) status has been given to xylitol by FDA (Food and Drug Administration) in 1986. Xylitol has shown very little toxicity issues through various routes of administration with negative results for tetrogenicity, embryogenicity and reproductive toxicity for mutagenicity and clastogenicity through in vivo and in vitro
FDA (1986) approved xylitol to be safe for human consumption and joint FAO/WHO Experts Committee on food additives also recommended safety levels of this polyol sugar with no need of further toxicological studies. Many previous studies conducted on rats and diabetic patients confirmed the safety levels of xylitol with no side effects in relation to carbohydrate and fat metabolism.\textsuperscript{30-32}

CONCLUSION

Diabetes is found to be an epidemic disease among the people of India resulting in loss of national productivity and exchequer at social level. The major factors responsible for this disease are obesity, food insecurity, illiteracy, poor sanitation, poor glycemic control and dominance of communicable diseases. Several oral drugs, amylin agonists, glucagon antagonists, protein tyrosine phosphatase inhibitors, salicylate derivatives and G protein coupled receptors are used to treat diabetes. However, these treatments are costly and associated with many side effects like allergic reactions, swollen ankles, weight gain, abdominal pain and digestive disturbances. Therefore, there is an urgent need to develop government policies, interventions and public awareness programmed in India to overcome the spread of this disease in the future generation. As an alternate natural sweetener, xylitol overcomes the spread of diabetes due to its metabolism independent to insulin. There are many constrains towards the use of this polyol sugar mainly the cost factor. Therefore, some biotechnological methods should be developed by utilizing low cost agrowaste material to increase the yield of xylitol in cost effective manner for its utilization in therapeutic sector.

REFERENCES


