Physiological Effects of Dietary Complex Carbohydrates and its Metabolites Role in Certain Diseases

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Abstract: Carbohydrate is one of the basic and an important food nutrient consumed worldwide. Likewise Pakistani foods contain more carbohydrates than any other food nutrient consumed. Sometimes, Pakistani foods are devoid of protein and may contain only carbohydrates and fats as the major nutrients of the diet e.g. eating chapati (wheat bread) with potato curry. Certain non-communicable diseases can be avoided with adoption of proper healthier food habits and eating foods according to the needs of the body. These diseases are obesity, coronary heart disease, colonic cancer and gastrointestinal disorders (diverticular disease, constipation, hiatal hernia and hemorrhoids). Therefore complex carbohydrate should be an important constituent of our daily meal and it can be adopted for the management of certain diseases provided that it is used in proper amounts. Consumption of certain complex carbohydrates is associated with lower body weight, reduced blood cholesterol, reduced blood glucose and an increased crypt cell proliferation. Therefore, it is necessary and utmost important to know the various types of carbohydrates to enable us to decide to include carbohydrates in our daily food according to our health requirements. Not necessarily all the community need to know but at least those who are associated with nutrition and health management must know the beneficial as well as the harmful effects of carbohydrates.

Key Words: Complex carbohydrates, fibres, digestion, absorption, metabolites short chain fatty acids, diseases

Introduction
What are the complex carbohydrates?: Complex carbohydrates refers to large molecular forms of carbohydrates (resistant starch and dietary fibres): are types of carbohydrates, which are not digested in the upper gastrointestinal tract and are fermented, in the large bowel by the action of various bacteria. The fermentation products are mainly short chain fatty acids (SCFAs) or volatile fatty acids (VFAs), methane (CH₄), hydrogen (H₂) and carbon dioxide (CO₂). The SCFAs produced from the fermentation are absorbed at site of production and transported to the liver via entero-hepatic circulation. The SCFAs play an important nutritional role that is discussed in the proceeding sections.

History and Definition of Complex Carbohydrates: In 1923 Kellogg and others stimulated the study of dietary fibre in the U.S.A. (Kellogg, 1923): however the term "unavailable carbohydrate" was used long before (McCance and Lawrence, 1929). The unavailable carbohydrate was later called "dietary fibre " (Hipsley, 1953) which was defined as "that portion of plant food resistant to hydrolysis by the alimentary enzymes of man" (Trowell, 1976). Kritchevsky (1988) defined as dietary fibres "plant material that resists digestion by human alimentary enzymes". It includes many different substances; with the exception of lignin, all are carbohydrate in nature. Chemically fibre was defined as "non starch polysaccharides (NSP)" (Cummings, 1981). The NSP include cellulose and non-cellulosic polysaccharides (NCP) (Kay, 1982). The latter includes pectin and hemicelluloses (structural polysaccharides); fructans, glucofructans, mannans and galactomannan (storage polysaccharides); gums and mucilages (isolated polysaccharides) containing a mixture of pentoses, hexoses and uronic acids (Kay, 1982) Apart from these lignin, protein, cuticular lipids and inorganic constituents, such as silica, magnesium, calcium and potassium are associated with the plant cell wall polysaccharides (Cummings, 1981). There is substantial evidence that some starch resists digestion in the upper gastrointestinal tract (GIT) and can act as a potential source of substrate for fermentation in the large bowel (Cummings and Englyst, 1987). This starch is known as resistant starch (RS) (Cummings and Englyst, 1987) and has been recently redefined as " the sum of starch and products of starch degradation not absorbed in the small intestine of healthy individuals". Due to various chemical substances which could contribute to dietary fibre early definitions were inappropriate and the British Nutrition Foundation's Task Force introduced a new term "Complex carbohydrates" which includes both NSP and starches (British Nutrition Foundation's Task Force, 1990). The insoluble complex carbohydrates are insoluble in water, non-viscous in nature and nearly hundred percent fermentable in large bowel whereas the insoluble complex carbohydrates are insoluble in water, non-viscous in nature and slowly fermentable in large bowel (Roberfroid, 1993). When these complex carbohydrates are eaten as a part of meal or fed to the experimental subjects behave differently and exhibit different physiological effects. For example, soluble complex carbohydrates may be helpful in the management of diabetes mellitus whereas the insoluble complex carbohydrates may be helpful in the management of constipation, diverticulitis, haemorrhoids and large bowel cancer (Gumaa et al., 2001; Muir et al., 1993). The classification based on it chemical nature is given in Table 1.

Types of Complex Carbohydrates: Generally, complex carbohydrates are grouped into two major types; i) soluble complex carbohydrates and ii) insoluble complex carbohydrates. The soluble complex carbohydrates are soluble in water, viscous in nature and nearly hundred percent fermentable in large bowel whereas the insoluble complex carbohydrates are insoluble in water, non-viscous in nature and slowly fermentable in large bowel (Roberfroid, 1993). When these complex carbohydrates are eaten as a part of meal or fed to the experimental subjects behave differently and exhibit different physiological effects. For example, soluble complex carbohydrates may be helpful in the management of diabetes mellitus whereas the insoluble complex carbohydrates may be helpful in the management of constipation, diverticulitis, haemorrhoids and large bowel cancer (Gumaa et al., 2001; Muir et al., 1993). The classification based on it chemical nature is given in Table 1.

Complex Carbohydrates and Certain Diseases: Several diseases have very close link with complex carbohydrates. These diseases are cardiovascular diseases, ulcer, dental caries, constipation, appendicitis, obesity, varicose vein, colorectal cancer and diabetes mellitus. To understand the link between these diseases and complex carbohydrates it would be essential to know the process of digestion of the complex carbohydrates and their end products of digestion and metabolism.

Digestion of Complex Carbohydrates: Most starch is digested in the small intestine with glucose as the absorbed product but some
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Table 1: Major types of non-starch polysaccharides (NSP)

<table>
<thead>
<tr>
<th>Primary Source of Plant Cell Wall</th>
<th>Major Group</th>
<th>Components Present</th>
<th>Summary of structures</th>
<th>Distribution in Foods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structural Materials</td>
<td>Cellulose</td>
<td>-</td>
<td>Long-Chain $\beta$-Glucans</td>
<td>Mainly in Fruits and Vegetables</td>
</tr>
<tr>
<td></td>
<td>Non-Cellulosic Polysaccharides</td>
<td>Pectic Substances</td>
<td>Galacturonans, Arabinogalactans</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hemicellulose</td>
<td>Arabinoxylan, Glucuron- Arabinoxylan</td>
<td>Cereals</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Glucuron-xylan, Xylo-glactans</td>
<td>Fruits and Vegetables</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>$\beta$-Glucans</td>
<td>Cereals</td>
</tr>
<tr>
<td>Non-Structural Gums</td>
<td></td>
<td>Wide Range of Hetro-Polysaccharides</td>
<td></td>
<td>Seed and Fruits</td>
</tr>
<tr>
<td>Polysaccharides</td>
<td></td>
<td></td>
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</tbody>
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Table 2: The principle substrates thought to be available for fermentation for large intestinal bacteria in a person consuming Western diets (Cummings and Macfarlane, 1991)

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Amount (g/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-starch polysaccharides</td>
<td>8-18</td>
</tr>
<tr>
<td>Resistant starch</td>
<td>8-40</td>
</tr>
<tr>
<td>Oligosaccharides</td>
<td>2-8</td>
</tr>
<tr>
<td>Unabsorbed sugars</td>
<td>2-10</td>
</tr>
<tr>
<td>Dietary protein</td>
<td>3-9</td>
</tr>
<tr>
<td>Pancreatic enzymes and other gut secretions</td>
<td>4-6</td>
</tr>
<tr>
<td>Mucus</td>
<td>2-3</td>
</tr>
<tr>
<td>Sloughed epithelial cells</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

Absorption of Metabolites of Complex Carbohydrates: Short chain fatty acids are absorbed in the monogastric animals including man via passive diffusion in a manner similar to that observed for rumen epithelium (Levrat et al., 1991; Fleming et al., 1991). Alternatively, it has been proposed that SCFA may be absorbed via anionic exchange (Ruppin et al., 1980; Argenzio and Southworth, 1977). Short chain fatty acids could be absorbed as un-dissociated acids (non-ionic diffusion), or sodium or potassium salts of short chain fatty acids (ionic diffusion) (Fleming et al., 1981; Ruppin et al., 1980; Argenzio and Southworth, 1977). The absorption has been shown to be accompanied by luminal increase in HCO$_3^-$ and decrease in CO$_2$, and by increased absorption of sodium, potassium and water. SCFA are most effectively transported at pHs lower than 7.0 and it has been proposed that in the human large intestine 60% of SCFA are absorbed in the un-dissociated acid form (Ruppin et al., 1980).

Energy contribution of SCFA in different species: Table 3 summarises estimates obtained in various species for the contribution of SCFA to the energy requirement of the whole body but this has been shown to vary with the type and amount of dietary intake. For example Ruppin et al. (1980) calculated that SCFA could supply 22% of the energy requirements in human subjects whilst other estimates (Cummings, 1981; Grossklaus, 1983; McNeil, 1984) are much lower at 2-7% based on 20 g of fibre fermentation daily.

Metabolism of SCFA: The SCFA are directly absorbed at the site of production and may be metabolised either locally in the gut, by the liver or by peripheral tissues. The SCFA absorbed may then be used for maintenance, growth and lipogenesis. The enzymatic activation of SCFA by formation of their respective acyl-CoA eg. acetyl-CoA, propionyl-CoA and butyryl-CoA are important factors regulating the rate of uptake of SCFA by different tissue (Bergman, 1990). Rat colonocytes have been shown to possess a butyryl-CoA synthetase which is more active than the acetyl-CoA and propionyl-CoA synthetases (Roediger, 1982). Most of the butyrate is usually oxidised to CO$_2$ and ketoine bodies in pig (Imoto and Namiokka, 1978), rabbits, (Marty and Verny, 1984), rats (Roediger, 1982) and humans (Roediger, 1982) by the colonic mucosa during its transportation to the bloodstream. Some of the propionate is also metabolised by the gut. The remaining butyrate, propionate and acetate are transported to the liver via
Table 3: Estimates of contribution of SCFA produced in different sections of the digestive tract of various species to energy requirements of the whole body

<table>
<thead>
<tr>
<th>Species</th>
<th>Organ</th>
<th>% of Energy requirements</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat</td>
<td>Caecum</td>
<td>5</td>
<td>Yang et al. (1970).</td>
</tr>
<tr>
<td>Pig</td>
<td>Large intestine</td>
<td>11</td>
<td>Imosi and Namioka (1978) and Kim et al. (1978).</td>
</tr>
<tr>
<td>Pig</td>
<td>Total hind gut</td>
<td>25</td>
<td>Rerat et al. (1987).</td>
</tr>
<tr>
<td>Pony</td>
<td>Caecum</td>
<td>30</td>
<td>Glinsky et al. (1976).</td>
</tr>
</tbody>
</table>

Fig. 1: Separation of plant carbohydrates

Fig. 2: Mechanism of action of NSP on blood cholesterol

Pearce, 1977). In rodents, lipogenesis occurs in both tissues. These differences in lipogenesis seem related to metabolism of acetate since acetyl-CoA can be easily incorporated into lipogenesis. In some studies it has been shown that hepatic acetate uptake is directly proportional to the concentration of acetate in the portal vein (Buckley and Williamson, 1977; Remesy et al., 1980). In ruminants, acetate carbon is incorporated into fatty acids by both adipose tissue and the mammary gland more rapidly than is glucose carbon (Ballard et al., 1969; Ballmain et al., 1954; Vernon, 1981) whereas in rats glucose is the preferred substrate (Ballmain et al., 1954). Acetate can be a significant source of fuel for skeletal muscles (Snoswell et al., 1982). However, the quantitative importance and the metabolic fate of acetate in the simple stomach species such as humans and rats are not well understood.

Metabolism of propionate: Propionate is partially metabolised by the gut epithelium and liver takes up most of the remainder. Propionate is the only SCFA that can be a major source of glucose; acetate, butyrate and longer chain SCFA with an even number of carbon atoms cannot contribute to net synthesis of glucose. This is because these SCFA are converted to acetyl-CoA only and the acetyl-CoA enters the tricarboxylic acid (TCA) cycle. When acetyl-CoA enters the cycle two carbon atoms are lost as CO₂, and there is no net gain of oxaloacetate and, therefore, no net glucose synthesis is possible (Weinman et al., 1957). The propionyl-CoA synthetase activity has been reported to be greater than acetyl-CoA synthetase activity (Ash and Baird, 1973 and Demigne et al., 1986) as a result of which most of the absorbed propionate is removed by the liver (Goodlad and Matthers, 1990; 1991). Once propionate is absorbed, it can be used for gluconeogenesis or for energy production via the TCA cycle. In
By reducing dietary cholesterol absorption through increasing the thickness of the unstirred layer and reducing transit time in the gut

By increasing the bile acid excretion in the faeces (by binding bile acids, increasing conversion of cholesterol to bile acids). By increasing the activity of enzyme 7-α-hydroxysterol in the liver

Reduced blood cholesterol concentration

By reducing cholesterol synthesis in the liver and small intestine, indirectly by inhibiting the activity of enzyme HMG-CoA-reductase in the liver and small intestine via the fermentation product propionate.

Fig. 3: Mechanism of action of NSP blood cholesterol

Proposed mechanisms of actions of Complex Carbohydrates: The proposed mechanisms by which dietary NSP reduce blood cholesterol concentration include physical effects for example increased digest viscosity, enhanced bile acid excretion and altered digestion and absorption of lipids (Topping, 1991) as indicated in the Fig. 3.
Reduced cholesterol synthesis: One of the leading hypotheses has been the inhibition of cholesterol synthesis in hepatocytes via the fermentation products SCFA (especially propionate) Illman et al., 1988. Thacker et al. (1981) and Thacker and Bowland (1981); Bolia et al., (1981) reported that feeding 5% propionic acid in the diet lowers blood cholesterol concentration in pig. It has also been reported that the addition of propionic acid at concentration of 15 and 30 mM to bovine liver homogenate inhibited HMG-CoA reductase activity (Bush and Milligan, 1971). These concentrations of propionate are very much higher than those found in vivo so the practical significance of these observations must be in question. With isolated rat hepatocytes propionic acid inhibits cholesterol and fatty acid synthesis using 14C-acetate, H2O and 14C-mevalonate as tracer (Ide et al., 1978). However, in human subjects, it has been shown that feeding sodium propionate at the rate of 7.5 g/d in a capsule form did not lower the serum total cholesterol but increased HDL cholesterol concentration (Venter et al., 1990).

Complex Carbohydrates enhance faecal bile acids excretion: The cholesterol lowering effect of dietary NSP could be predominantly because of the interruption of the bile acid circulation (enterohepatic cycle). Studies with dietary guar gum in rats have been shown that the activity of the enzyme 7α hydroxase (EC 1.14.13.17) which is the rate limiting step in the conversion of cholesterol to bile acids in the liver is increased and at the same time there is increased faecal bile acid excretion (Ide et al., 1990). It has been observed that other dietary NSP increase the 7α-hydroxase activity in the liver of rats and decrease the bile acid pool (Ide et al., 1990; Marcus and Heaton, 1986; Arjmandi et al., 1992; Turkley et al., 1991). In hyperlipidaemic subjects 40-50 g of pectin/d reduced blood cholesterol concentration; this decrease was associated with the increase in cholesterol elimination of bile acid in the stool which is then balanced by enhanced cholesterol synthesis (Arjmandi et al., 1992; Ebihara and Schneeman, 1988; Story, 1985). In this respect, soluble NSP act in similar way to the bile acid sequestrant such as cholestyramin but this effect is associated with the type of NSP fed to the experimental subjects (Turner et al., 1990). Similar effects have been observed in vitro with different dietary NSP sources on bile acids (Story and Kritechekvsky, 1976).

Viscosity and transit time: The ingestion of soluble NSP increases the viscosity of the contents of the stomach and small intestine and therefore might interfere with digestion and absorption of lipids (Topping et al., 1988 and Blackburn and Johnson, 1981) in similar way to that described earlier.

Effect of NSP on Crypt Cell Proliferation (CCP): There is substantial evidence in the literature that soluble NSP sources increase epithelial cell proliferation in the gut (Pell et al., 1992; Lupton et al., 1988) but the mechanism for this effect is not established. There seems to be many different mechanisms involved simultaneously in increasing the intestinal CCP, such as the increased delivery of organic matter (OM) to the large bowel (Mathers et al., 1993). The increased supply of OM to the large bowel stimulates bacterial fermentation resulting in increased SCFA production and a more acidic pH. Increased concentration of SCFA and reduced pH may be responsible for the elevated CCP (Lupton and Kurtz, 1993). Sakata (1987) reported that CCP was stimulated in the caecum and colon by butyrate injection into the caecum. Goodlad et al., (1989) reported that dietary NSP sources increase the CCP in the small intestine and colon in conventional rats whereas CCP was not affected in germ-free animals and concluded that it is the fermentation product which increase the cell proliferation. Another, mechanism by which the soluble NSP may influence intestinal cell growth is through the binding of luminal inorganic ions (James, 1980), such as calcium, which is considered to be important in the control of cell proliferation (Durham and Walton, 1982). Soluble NSP bind bile acids which have been shown to damage the mucosal cell surface causing higher rates of cell sloughing and resulting in compensatory stimulation of cell synthesis (Jacobs and Lupton, 1984). It has been shown that hormones play an important role in the regulation of epithelial cell proliferation and soluble NSP affect gut hormones such as entero-glucagon and gastrin (Pell et al., 1992; Winsette et al., 1986).

Conclusions: Consumption of certain complex carbohydrates is associated with lower body weight, reduced blood cholesterol, reduced blood glucose and an increased crypt cell proliferation. A possible mechanism of action is related to viscosity and gel forming abilities.

References


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