Effect of prolonged consumption of gari (Cassava, Manihot Utilisima) on rat hepatic energy metabolism

1. Mitochondrial respiratory control

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Abstract. Rats were fed high (35%, w/w) gari (Cassava, Manihot utilisima) - based diets for a prolonged period and sacrificed after 22/23 days, 30/31 days, 45/46 days and 59/60 days. Hepatic mitochondrial respiratory control for succinate oxidation was evaluated by four criteria (a) osmotic swelling/contraction cycle, (b) oxygen uptake, (c) ATPase activity and (d) Ca\(^{2+}\) uptake. A decrease (28-51% in respiratory control ratio (RCR)) in the degree of oxidative phosphorylation coupling, ATPase activity (19-24%) and increased swelling/contraction (30-75%) with no apparent effect on Ca\(^{2+}\) uptake were suggestive of moderate alterations in mitochondrial energy metabolism caused by the ingestion of gari based diet. The possible in vivo significance of these observations are discussed.

Introduction

Dietary manipulations, xenobiotics and malnutrition are well recognised modulators of in vivo metabolic activities in all biological systems which may result in a new (or altered) steady state metabolism either pathologic or still compatible with a feeling of well being.

Gari, a starchy Nigerian staple food, is prepared from cassava (Manihot utilisima) tubers. Its hepatotoxicity, neurotoxicity and goitrogenicity are reported to be caused by its content of the cyanogenic glycosides linamarin (phaseolunatin) and methyl linamarin (lotaustralin) present in cassava [1-3]. 'Prepared' or (cooked) gari may contain as much as 25 mg of hydrocyanic acid (HCN) in an average daily consumption of 750 g [4].

Recent studies have shown an increase in the glycogen content of the livers of rats fed on cassava [5]. An impairment in glycogen mobilization was suggested which possibly was an indication of altered energy metabolism with or without endocrine involvement.

Because cyanide is a potent respiratory (cytochrome oxidase) inhibitor [6] there has inevitably been speculation whether chronic pathological changes in mitochondrial energy metabolism might arise from prolonged intake of sublethal doses of dietary hydrocyanic acid. Cyanide is detoxified in the body to thiocyanate by a mitochondrial sulphurtransferase, formerly
called rhodanese [6]. There is also substantial evidence that hydroxocobalamin (vitamin B<sub>12</sub>) plays a more active role in cyanide detoxication [7]. Subsequent enzymatic decyanation of cobalamin requires adequate supplies of nicotinic acid and riboflavin [8]. Since Clark in 1936 had proposed that both HCN and suphite (derived from thiosulphate) inactivated thiamine [9] it is logical to infer that prolonged intake of cyanide will probably deplete the body's stores of these vitamins when dietary intakes are marginal. It is also significant that these vitamins of the B-complex are components of coenzymes of energy and neurotransmitter metabolism and their deficiencies characterized by degenerative changes in the nervous system are well documented [10].

In the absence of any experimental evidence for the cumulative effect of HCN on cytochrome oxidase system [7] we have investigated the effect of prolonged consumption of gari on rat hepatic mitochondrial respiratory control and other associated energy linked functions.

**Methods**

*Preparation of control and experimental rat feeds*

The percentage compositions of the control and experimental feeds are given in Table 1.

<table>
<thead>
<tr>
<th>Food items</th>
<th>Control</th>
<th>Experimental</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gari</td>
<td>35</td>
<td>67</td>
</tr>
<tr>
<td>Maize flour</td>
<td>23</td>
<td>32</td>
</tr>
<tr>
<td>Groundnut cake</td>
<td>10</td>
<td>23</td>
</tr>
<tr>
<td>Fish meal</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

All food items were purchased from the local market at Nsukka, ground up in a commercial mill and the wet mixture pelleted by hand and finally sun dried. The gari incorporated into the experimental feed mixture was first prepared as traditionally eaten. A quantity of the raw gari was poured into a bowl of boiling water, excess water and coarse gari particles were then drained off as waste. The so 'prepared' so cooked gari, slightly hardened with cooling, was kneaded into a dough, pelleted and sun dried before milling. This method of preparation ensures further decyanation of the gari before human consumption as Table 2 shows [4]. It is pertinent to mention that earlier investigators did not decyanate the gari as traditionally practised before incorporating it into experimental feeds and therefore the toxicological consequences were not accounted for in their studies.