Hypothesis
Silicon, Fibre, and Atherosclerosis

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Summary A logical argument can be made for the hypothesis that lack of silicon may be an important aetiologic factor in atherosclerosis. As silicic acid or its derivatives, silicon is essential for growth. It is found mainly in connective tissue, where it functions as a cross-linking agent. Unusually high amounts of bound silicon are present in the arterial wall, especially in the intima. Various kinds of dietary fibre have been reported to be effective in preventing experimental models of atherosclerosis, reducing cholesterol and blood-lipid levels, and binding bile acids in vitro. Exceptionally large amounts of silicon (1000 to 25000 p.p.m.) were found in fibre products of greatly varying origin and chemical composition which were active in these tests. Inactive materials, such as different types of purified cellulose, contained only negligible quantities of the element. It is concluded that silicate-silicon may be the active agent in dietary fibre which affects the development of atherosclerosis. Two out of three samples of bran also had relatively low levels, which could explain why bran does not lower serum-cholesterol. The fact that atherosclerosis has a low incidence in less developed countries may be related to the availability of dietary silicon. Two instances are presented where silicon is reduced by industrial treatment; white flour and refined soy products were much lower in silicon than their respective crude natural products. The chemical nature of silicon in different types of fibre is not known. It could exist as orthosilicic acid, polymeric silicic acid, colloidal silica (opal), dense silica concretions, or in the form of organically bound derivatives of silicic acid (silanolates). Possible mechanisms of action are discussed.

INTRODUCTION

In 1972 we demonstrated, by means of a plastic trace-element-sterile isolator system and highly purified aminoacid diets, that silicon (as silicic acid or its derivatives), is an essential element.' In rats fed silicon-deficient diets, supplements of metasilicate enhanced the rate of growth by 35%. Similar observations were made on chicks.' Silicon deficiency is accompanied by bone deformities.' The element is found mainly in connective tissue, where it functions as a cross-linking agent of the ground matrix. 5 Fractionation studies showed that it is bound to mucopolysaccharides, such as hyaluronic acid and chondroitin-4-sulphate, and also to collagen. 6 It appears to be present as an ester (or ether-like) derivative of silicic acid, forming -O-Si-O- bridges and thus contributing to the architecture and strength of connective tissue and membranes.' The silicon atom is eminently qualified as a cross-linking agent: it is a small atom with the same stereochemistry as carbon but with much greater rigidity in maintaining its bond angles. Unusually high amounts of bound silicon are found in the arterial wall, especially the intima. 7 In earlier work, Loeper and collaborators...
found that silicon levels were greatly reduced in atherosclerotic arteries. An inverse relation exists between the degree of atherosclerosis in the arterial wall and its silicon content. 8-10 More recently beneficial effects of silicate in drinking-water have been described on blood-lipid levels and cholesterol metabolism. 11-12 A coherent argument can thus be made for the hypothesis that lack of biologically available silicon in modern diets may play a part in the etiology of atherosclerosis, and silicon may exert a protective effect against this disease.

The role of dietary fibre in the prevention of atherosclerosis and other chronic diseases has recently attracted attention. 13-14 The idea originated over 20 years ago from a comparison of diets and disease patterns in Africans and Westerners, 15-17 from findings in the U.S.A. of lowered serum-cholesterol levels in vegetarians, 18-19 and from a comparison of the diets of Italians and Americans, in whom small but significant differences in serum-cholesterol were related to pectin. 20 Earlier, the action of pectins in the human and dog intestine had been analysed, and changes in the metabolism and excretion of cholesterol had been noted. 21-22 More pronounced and consistent effects were observed under experimental conditions, as first described by Wells and Ershoff in 1961. 23 Rats, chicks, rabbits, pigs, and also primates, including man, were used, and not only cholesterol and blood-lipid levels but also experimental models of atherosclerosis were found to be beneficially affected. Recently, in-vitro bile-acid binding has been applied as a method to study the action of fibre-containing products. Comprehensive reviews are available. 24-27

"Dietary fibre" is poorly defined chemically. It designates constituents of food which are resistant to digestion. This comprises not only cellulose but also hemicelluloses, pectins, other polyuronides, gums, mucilages, lignin etc. Many studies have been published on the effects of these products on blood cholesterol and lipid levels and on experimental models of atherosclerosis. Cellulose, per se, was without influence on serum-cholesterol in all tests except one. 28 Indeed, in some of these studies cellulose functioned as a filler or placebo. 29-30 Since only certain types of fibre are effective under various experimental conditions, it seems inappropriate to speak about "fibre" in general as a hypocholesterolaemic agent.

We have analysed a variety of products belonging to the category of dietary fibre. The results indicate that an exceptionally high amount of silicon is a common denominator of seemingly unrelated components of dietary fibre and other products which have been reported to be effective in lowering cholesterol and lipid levels, preventing experimental atherosclerosis, or binding bile acids in vitro.

METHODS

Silicon analyses were performed after ashing by sodium-carbonate fusion in platinum crucibles, using the colorimetric method of Baumann 32 High-purity chemicals, plastic laboratory ware, and silicon-free water were used throughout. Precautions were taken to eliminate the possibility of contamination by dust. Results are expressed as parts per million (P.P.M.) of silicon per dry-weight.

RESULTS

Various kinds of purified cellulose were very low in silicon (see table, nos, 1-3), and cotton, considered the purest natural form of cellulose contains only 120 p.p.m. Other samples of fibres (except two specimens of bran) had exceedingly high levels, despite their diverse biological and geographical origins. Values ranged from approximately 1000 to over 25000 p.p.m. These amounts are quite large compared to those in tissues and parenchymal organs, which are normally in the range 2-30 p.p.m. 33 Except for lungs and lymph-nodes, only connective tissue often exceeds 100
# SILICON IN DIETARY FIBRE

<table>
<thead>
<tr>
<th>Silicon (ppm of dry weight)</th>
<th>Sample</th>
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<tbody>
<tr>
<td>6</td>
<td>14. Wheat bran Æ</td>
</tr>
<tr>
<td>6</td>
<td>15. Wheat bran §</td>
</tr>
<tr>
<td>50</td>
<td>16. Wheat flour (65% extraction) §</td>
</tr>
<tr>
<td>116</td>
<td>17. Soybean meal ¶</td>
</tr>
<tr>
<td>23110</td>
<td>18. Soya fluff</td>
</tr>
<tr>
<td>11270</td>
<td>19. Nutrisoy flour **</td>
</tr>
<tr>
<td>12740</td>
<td>20. Citrus pectin N.F. *</td>
</tr>
<tr>
<td>27300</td>
<td>21. Lemon pectin ÆÆ</td>
</tr>
<tr>
<td>22500</td>
<td>22. Na-polypectate ÆÆ</td>
</tr>
<tr>
<td>16910</td>
<td>23. Na-pectate, enzymatically de-esterified ÆÆ</td>
</tr>
<tr>
<td>7140</td>
<td>24. Guar gum *</td>
</tr>
<tr>
<td>12240</td>
<td>25. Curry powder §§</td>
</tr>
<tr>
<td>1720</td>
<td>26. Chondroitin-4-sulphate ¶¶</td>
</tr>
</tbody>
</table>

* Dr P. Griminger, Rutgers University, New Brunswick, New Jersey.
Æ Dr D. Krilchevsky, Wistar Institute, Philadelphia, Pennsylvania.
Æ Kruse Grain & Milling, El Monte, California; samples washed twice with 1:1 EtOH-CHCl₃ solution before analysis.
§ American Institute at Baking, Chicago, Illinois.
¶ Cargill, Inc., Minneapolis, Minnesota; solvent-extracted, 48.5% protein.
|| E. C. Young, Co., Los Angeles, California.
** Archer Daniels Midland Co., Los Angeles, California.
ÆÆ Dr R. McCready, Western Regional Laboratories, Berkeley, California.
ÆÆ Sunkist Growers, Ontario, California.
§§ Spice islands, San Francisco, California.
¶¶ Institute of Atherosclerosis Research, Los Angeles, California.

Some of the items analysed (see table) were obtained from other institutes, where they had been assayed for various effects: crude fibre products (nos. 5, 6, 10, 12, and 13) have been studied by Story and Krilchevsky for their potential to bind bile-acids in vitro. 34 All were effective, except for wheat straw, and all showed high amounts of silicon. The same authors have found curry powder to be quite active in bile-acid binding; 35 a commercial sample (no. 25) showed 1800 p.p.m. of silicon. The National Formulary pectin (no. 20) and the guar gum (no. 24), in both of which high amounts of silicon were detected, have been used by Griminger and Fischer in studies of cholesterol levels in chicks. 36 In five other citrus pectins not shown here values ranged from 1100 to 2590 p.p.m. We reported previously that pectin contains large amounts of silicon. Stability tests indicated that it is present as an organically bound form of silicic acid, an organosilicate. 5 However, commercial pectins are often contaminated with microscopic and colloidal silica. Chemical modification of pectin did not significantly alter the silicon levels found (nos. 21-23), The sample of chondroitin-4-sulphate (no. 26) is representative of many similar specimens studied in our laboratory. Extensive clinical trials showed beneficial effects on atherosclerosis, 37 A large amount of silicon was found, in accordance with our previous report, in chondroitin sulphates and other glycosaminoglycans, 5

**DISCUSSION**
Different kinds of dietary fibre might affect chronic diseases through a variety of mechanisms. Fibre might change fatty-acid absorption, bacterial flora, formation of volatile fatty acids, intestinal-transit time, and consistency of faeces. It also counteracts toxic effects. Its mode of action in atherosclerosis could clearly be different from the mechanisms which have been invoked in the prevention of other diseases - e.g., diverticulitis and cancer of the colon.

Large amounts of silicate-silicon (1000-25000 p.p.m.) are present in very different kinds of dietary fibre which lower serum cholesterol and lipid levels or prevent experimental atherosclerosis or bile-acid binding. Conversely, types of fibre which are inactive in such tests (e.g., cellulose) contain only negligible quantities of the element. The influence of natural fibre on atherosclerosis obviously does not depend on cellulose itself, for fibre products containing no cellulose are also effective in various trials. Since a high silicon content is characteristic of the active products, silicate-silicon may be the crucial ingredient in these materials.

The much lower incidence of atherosclerosis in less developed parts of the world than in industrialised areas may be related to the availability of silicon in the diet. Skin, cartilage, tendon and other part of animal origin which are rich in silicon may be used less efficiently for human consumption in developed countries; in addition, the intake of fibre of plant origin is reported to be much lower. Industrial refinement can greatly reduce the amount of silicon in foods; samples (nos. 15 and 16) of amount of silicon bran and wheat flour were prepared by carefully controlled milling of a specific lot of wheat. 65%-extraction flour contained less than 10% of the silicon found in bran. Soybean meal (no. 17), a source of fibre which reduces blood-lipids and experimental atherosclerosis, 38 was high in silicon, but two refined soybean preparations for human consumption (nos, 18 and 19), contained very little of the element.

Bran samples of different origin (nos, 13 - 15) varied significantly in silicon content, two out of three specimens having low values. Such differences may be related to the kind and origin of the grain and to differences in the milling process. They could account for discrepancies in the results obtained with bran by different investigators. 39-40 Whereas some authors have seen effects on blood-lipids in experiments with bran supplements, others have found bran ineffective in lowering serum-cholesterol, despite its popularity. Indeed, there appears to be no report which states that bran lowers serum-cholesterol levels in man. There are similar inconsistencies in the reported effects of cellulose. Whereas the purified preparations analysed by us were very low in silicon, other cellulose specimens, of different origin may contain higher amounts. 2

The chemical nature of silicon in the various types of fibre investigated here is not exactly known. In plants it exists as orthosilicic acid, polysilicic acid, colloidal silica (opal), and also as dense silica (SiO2 ) concretions (phytoliths). Hard woods may contain over 0 5% of SiO2 , 41 Organically bound forms of silicic acid also play a part - for instance, in straw, where galactose has been implicated as the site of silicate binding. 42 Various forms of silicon in different categories of fibre obviously may differ in availability. Different forms of silicic acid and polymerised silica (SiO2 ) vary in their absorbability in the gastrointestinal tract. 43 In our experience the organosilicates - i.e., esters of silicic acid - appear to be utilised best for growth in the rat. 7

Several mechanisms could be involved in beneficial effects of silicate-silicon on atherosclerosis:

1. Various forms of polymeric silicic acid or silica could be the site of bile-acid
binding in the digestive tract, which would enhance the elimination of metabolic end-products of cholesterol; binding of cholesterol itself caused also play a part. This concept is supported by studies which showed that addition of silicic acid to drinking-water caused a significant reduction of serum cholesterol and lipid levels, enhanced excretion of tritium-labelled cholesterol and its conversion products in the faeces, and reduced the uptake of labelled cholesterol in liver, spleen, and kidney. 11-12

2. Silicic acid of other biologically forms of silicon (organosilicates) could be absorbed and function in the organism as essential constituents of connective tissue. They would thus contribute to the integrity and stability of the arterial wall.

3. An activated form of silicic acid could participate directly (in the intermediary metabolism of steroids and bile acids.

The observations reported here may also be related to the water factor -i.e., the constituent of hard water which seems to exert an inhibitory effect on coronary heart-disease. 44-45 We have found an inverse relation between silicic acid in drinking-water and the prevalence of coronary heart-disease in Finland, 46 suggesting once again that lack of silicon may be an ætiological factor in atherosclerosis.

The expert technical assistance of Mrs Billie A. Ricci is gratefully acknowledges. I thank Dr P. Griminger, Dr D. Kritchevsky, Dr R. McCready, Dr L. Morrison, and Mr Jerry Wilson for supplying samples of fibre.

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DR SCHWARZ : REFERENCES

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45. *WHO Chronide,* 1972, 26, 51.

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<td>2. Cellulose, Whatman F-11</td>
<td>6</td>
<td>15. Wheat bran §</td>
<td>229</td>
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<td>3. Filter-paper, Whatman No.1</td>
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<td>16. Wheat flour (65% extraction) §</td>
<td>21</td>
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<td>4. Cotton, pure, sterile</td>
<td>116</td>
<td>17. Soybean meal ¶</td>
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<td>5. Sugar beet pulp Æ</td>
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