

Letter to the Editor

Sorbitol, an Inhibitor of Intestinal Absorption of Vitamin B₁₂

Dear Sir:

During the last two years several papers were published in *Nature* and *The American Journal of Clinical Nutrition* concerning the augmenting effects of sorbitol on serum vitamin B₁₂ levels and on the intestinal absorption of radioactive vitamin B₁₂. Most of these studies were performed in human beings and rats with unphysiologically high doses of vitamin B₁₂ and the results were partly unreproducible in other laboratories.

Therefore, we think that it might be of some interest that studies in our laboratories have demonstrated that sorbitol and other carbohydrates are also potent inhibitors of intestinal absorption of vitamin B₁₂ and of intrinsic factor in human beings, pigs, rats and guinea pigs if physiologic test doses of radioactive vitamin B₁₂ are used.²⁻⁴

In studies in human beings (⁶⁰Co-vitamin B₁₂ test dose: 0.5 μg.; urinary and faecal excretion test) it was never possible to demonstrate therapeutically significant augmenting effect of sorbitol on absorption of vitamin B₁₂.^{2,3} In 30 per cent of the cases administration of 10 gm. L-sorbose or D-sorbitol had an inhibiting effect in normal subjects, partly reducing the intestinal absorption of vitamin B₁₂ to the range of pernicious anemia or sprue. This inhibition could be compensated by intrinsic factor in some patients.^{3,5} Increasing the dose of sorbose or sorbitol to 30 to 50 gm. is followed in nearly all patients by a reduction of the absorption of vitamin B₁₂ which is no longer reversible by intrinsic factor.³

In patients with pernicious anemia in remission administration of 10 to 30 gm. of sorbitol interferes with the effect of intrinsic

factor on absorption of vitamin B₁₂. For example, the biologic activities of 24 mg. of an Organon intrinsic factor preparation or 5 mg. of a Lederle intrinsic factor concentrate were reduced to 50 per cent after simultaneous oral administration with 0.5 μg. ⁶⁰Co-vitamin B₁₂ and 10 gm. sorbitol.^{6,7} The inhibitory action of sorbitol on the intestinal absorption of vitamin B₁₂ was compensated by increasing the doses of intrinsic factor to 400 per cent of the values mentioned. However, it was not possible to bring the absorption of vitamin B₁₂ back to normal values after sorbitol-inhibition in all patients, especially if higher sorbitol doses (30 to 50 gm.) were used.

Studies in pigs also demonstrated a considerable inhibitory action of 20 gm. L-sorbose on the absorption from an oral test dose of 0.5 μg. ⁶⁰Co-vitamin B₁₂.³⁻⁵

A publication from Castle's laboratories on studies in rats clearly shows that administration of an elixir containing 28 per cent sorbitol did not show any improving effect on the absorption of vitamin B₁₂ if physiologic test doses of vitamin B₁₂ were used in intact or in totally gastrectomized rats.¹

Recently other studies on the absorption of ⁶⁰Co-vitamin B₁₂ from intestinal loops of the rat have presented evidence that sorbitol in high concentration interfered with the absorption of vitamin B₁₂ and that the absorption in rats was still reduced after completion of several months of sorbitol feeding.⁹

In human beings absorption of vitamin B₁₂ was still within the range of pernicious anemia sometimes two to three days after a few single oral doses of sorbose or sorbitol.^{3,5}

Studies in guinea pigs with a physiologic oral

test dose of 30 ng. ^{60}Co -vitamin B_{12} demonstrate that the inhibitory effect of sorbose on the intestinal absorption of vitamin B_{12} is approximately proportional to the logarithm of the amount of sorbose administered (between zero and 1,500 mg. sorbose).^{3,5} Indeed, administration of 100 mg. sorbose proved to have an inhibiting action.

Recent unpublished work on the structural specificity of the inhibitory effect of sorbitol on the intestinal absorption of vitamin B_{12} has shown that other carbohydrates also diminish the absorption of vitamin B_{12} in guinea pigs and rats. Only one, D-fucose, was a much more potent inhibitor than D-sorbitol and none of the tested compounds showed an augmenting effect.^{7,8}

The mechanism of action of the inhibitory effect of carbohydrates was studied *in vitro* with a radio-paper-chromatographic technic.^{3,5} Sorbitol, sorbose and other carbohydrates, which interfere with absorption of vitamin B_{12} , form a complex with ^{60}Co -vitamin B_{12} , but between 5 and 40×10^6 molecules of the carbohydrate are required for the binding of a single molecule of vitamin B_{12} . Within reasonable concentrations sorbitol does not interfere with the *in vitro* binding reaction between vitamin B_{12} and intrinsic factor.⁷ From these observations, and since sorbitol is absorbed and metabolized very rapidly in human beings, it is supposed that the mechanism of action of sorbitol and related compounds is in some way connected with the fixation of the vitamin B_{12} -intrinsic factor complex to the surface of the absorbing intestinal mucosa.

There is no reason to believe that sorbitol could be a substitute for Castle's intrinsic factor and as such augment intestinal absorption of vitamin B_{12} . Repeated administration of high doses of sorbitol in therapy or nutrition, either in human beings or in animals, may produce an

inhibition of intestinal absorption of vitamin B_{12} and may ultimately result in the development of a vitamin B_{12} deficiency.

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