XLVII. A NOTE ON THE CONSERVATION OF THE POTENCY OF CONCENTRATED ANTISCORBUTIC PREPARATIONS.

By SYLVESTER SOLOMON ZILVA.

From the Biochemical Department, Lister Institute, London.

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SOME years ago it was shown that decitrated lemon juice prepared in concentrated form was of therapeutic value in the treatment of infantile scurvy [Harden, Zilva and Still, 1919]. The advantage of such a treatment is that very potent antiscorbutic solutions can be administered in very small bulk without introducing at the same time most of the extraneous matter present in active juices derived from natural products. During the last few years the writer had had the opportunity of preparing on a number of occasions concentrated decitrated lemon juice solutions which were used with great success in cases of acute infantile scurvy. These preparations were found to be especially of great value when the patients were suffering from gastric disturbances which made the administration of ordinary antiscorbutics difficult. As an example of this one may quote a recent case of Dr G. F. Still at the Hospital for Sick Children, Great Ormond Street, to whom I am indebted for the following particulars.

Patrick M..... Age 10/12. Admitted Jan. 29, 1923.

Tenderness of limbs since November. Fed on Allenbury foods, No. 1 till 4 months, No. 2 till 7 months, No. 3 (made with milk) until December when he was put back during the last 2 or 3 weeks to No. 2. Has also had some oatmeal water but nothing else.

On admission did not move arms or legs. Screamed with pain when arms or legs touched, especially wrists and ankles; some thickening just above ankles and wrists; apparently periosteal haemorrhage; haemorrhages into gums around incisors; urine, no blood; temperature varying up to 103·4° F.

Treated with potato cream and orange juice; one teaspoonful of each twice a day.

After 6 days, child more comfortable but temperature irregular.

Orange juice given four times daily. By February 5th stools became frequent, green, and loose, and from this time, although the child became much less tender, the looseness of the bowels, with much mucus, continued; there was no naked eye blood in the stools.

By February 19th the child was looking very bad; temperature 104°, eyes sunken, and looked as if likely to die. The ordinary antiscorbutics had been stopped on account of the bowel condition.

Concentrated decitrated lemon juice begun on February 21st; temperature reached normal on February 22nd, rose to 101° F. on 23rd and then fell to normal or thereabouts; the stools steadily improved.

The concentrated lemon juice was continued until March 5th $\frac{5}{8}$ iii per diem, except from February 21-25 when $\frac{1}{2}$ oz. was given daily; on the first day of an eight times concentrated solution (of which 2 oz. = 15 lemons), and on the second day a ten times concentrated solution, $\frac{1}{2}$ oz. was given.

The child continued to do well and gained weight during the next four weeks during which the periosteal thickenings gradually diminished until they had almost gone altogether.

No further trouble occurred, except that there was a gastro-intestinal disturbance a few days before the child was discharged from the Hospital on April 12th, but this did not appear to be connected in any way with his scurvy.

Such concentrated decitrated solutions, however, deteriorate in potency on keeping and consequently must be freshly prepared before administration—a circumstance which militates against their general use in medical practice. In view of the observations made by the writer on the inactivation of the antiscorbutic factor, conditions have been worked out which make it possible to store such concentrated antiscorbutic solutions without detriment to their activity. As it was found [Zilva, 1923] that destruction of the antiscorbutic factor is favoured by alkalinity and exposure to air, the concentrated antiscorbutic solutions were acidified and stored under anaerobic conditions. A concentrated juice stored in this way did not show any perceptible loss in potency after storage for three months.

Two and a half litres of lemon juice were treated with an excess of calcium carbonate and three volumes of absolute alcohol and filtered. The filtrate was concentrated to a tenth of its volume and acidified slightly. It was then stored in an ordinary conical flask in an evacuated bell-jar over alkaline pyrogalllic acid for three months. At the commencement of the experiment a suitable quantity of the concentrated juice was diluted to its original volume and tested out on guinea pigs in order to determine its minimum protective dose. During the period of testing (about six weeks) the diluted juice was also kept under an evacuated bell-jar over alkaline pyrogalllic acid, the necessary dose being removed daily. The concentrated and diluted preparations were kept at ordinary room temperature. At the end of three months another quantity of the concentrated preparation was diluted and tested out in the same way as at the commencement. As anticipated no loss of potency was observed. In both cases a daily dose of 1.5 cc. of the preparation which was previously diluted to its original volume afforded protection, whilst daily doses of 0.5 cc. and 1 cc. of both the original and stored preparation only protected the animal partially, the onset of the disease and death being delayed.

Adopting the above principle a method is now being worked out for the preparation of stable concentrated antiscorbutic solutions which could find practical application in the prophylaxis and treatment of infantile and adult scurvy and which it is hoped will be of use to the clinician.

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REFERENCES.

- Harden, Zilva and Still (1919). *Lancet*, i, 17.
Zilva (1923). *Biochem. J.* 17, 410.