

units, respectively. The estimated decrease in vitamin A potency of the oleovitamin A and D oils during the exposure test were practically identical, being 808, 814 and 802 units, respectively, for the cottonseed, peanut and corn oil preparations. The decrease in potencies of the cod-liver oils was estimated to be 375 and 1767 units/Gm., respectively, for samples 4 and 5. The difference in the vitamin A loss in the two cod-liver oil samples is doubtless influenced by the marked difference in the vitamin A potency of the samples. However, the average loss of vitamin A, 46.64%, for the cod-liver oil samples is only about half the loss, 80.80%, for the oleovitamin A and D products. Apparently the vitamin A in cod-liver oil is protected to some extent by an antioxidant in the cod-liver oil or it is in a more stable form than that which was dissolved in the vegetable oils.

SUMMARY

Samples of oleovitamin A and D prepared with cottonseed, peanut and corn oils and samples of medicinal cod-liver oils were

exposed to early winter sunshine and sky-shine for 11 days to compare the permanency of their vitamin A content.

Vitameter assays were made of the vitamin A content of the oleovitamin A and D oils and of the cod-liver oil samples before and after the exposure test. The results of these tests showed that there was approximately 80% loss of the vitamin A content of the oleovitamin A and D, regardless of whether cottonseed, peanut or corn oil was used as a diluent. The loss of vitamin A from the cod-liver oils was only about one-half the vitamin A loss from the oleovitamins. Possibly cod-liver oil may contain some natural antioxidant or its vitamin A content may be in a more stable form than that of the vitamin A concentrate incorporated in the vegetable oils, used for preparing the oleovitamin oils employed in this study.

REFERENCES

- (1) "United States Pharmacopœia, XII," 1942, p. 311.
 (2) Holmes, A. D., and Remington, R. E., *Amer. J. Dis. Child.*, 49 (1935), 94.
 (3) Holmes, A. D., and Remington, R. E., *Ind. Eng. Chem.*, 26 (1934), 573.
 (4) Holmes, A. D., and Pigott, M. G., *Boston Med. Surg. J.*, 195 (1926), 263.

Zinc Peroxide*†

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The substances called zinc peroxide have been known and used in medicine for years. Since Thenard, in 1818, first produced (1) his "deutoxyde de zinc" by the action of zinc hydroxide and hydrogen peroxide, many others have prepared similar materials and by like processes, but almost always to yield products with somewhat differing composition. All of them contained zinc, oxygen and hydrogen in variable proportions, but hardly any two yielded the same results in elementary analysis, and this has been true often in two substances made by almost identical methods. This may perhaps explain the markedly inconsistent results in thera-

peutic application since introduction into practice 40 years ago. However, more recent reports would seem to indicate that, providing a zinc peroxide is used that is proved to contain maximum activity, excellent results can be obtained in arresting lesions caused by all types of anaerobic organisms.

EXPERIMENTAL

Because no one here has ever prepared a compound of the formula ZnO_2 or any other peroxide that contained no hydrogen, the present experiments were instituted to learn if such a compound can exist. In an extensive series, pure zinc oxide was subjected to oxygen at temperatures of 100° to 1000° C. but in every case the oxide was found unchanged analytically after treatment, and no evidence of active oxygen could be found in the residue.

The attempt was next made to attain peroxida-

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tion by means of nascent oxygen, using the notable instability of silver oxide as the source. Mixtures of this with zinc oxide were subjected to temperatures up to 220° C. at which point samples of silver oxide are all decomposed. In no case, however, was the residue found to contain active oxygen.

The results with ozone were somewhat difficult to interpret. Oxygen containing ample ozone from an ozonizer was passed through zinc oxide at several temperatures up to 100° C. In all cases the residual material liberated no iodine from a solution of potassium iodide, but did so if the solution was acidified, which is characteristic of ozone itself. Also, when talc or lime was employed in place of zinc oxide, the same result was obtained. It would seem that occlusion of the ozone had occurred in all of the powders. This was partly confirmed by the fact that the residue from zinc oxide was found by analysis to contain as great a percentage of zinc as at the start. Furthermore, heat apparently removed the active oxygen at slightly over 100° C.

It was also found that an active material was not produced by interaction of the oxide or chloride of zinc and benzoyl peroxide. The former was shaken with the latter in absolute alcohol, but in no instance was the insoluble residue able to liberate iodine from potassium iodide.

From the results of our experiments, we conclude that a compound corresponding to the name zinc peroxide does not exist at ordinary or higher temperatures. The commercial products so labeled all contain hydrogen and would appear to be physical, or possibly chemical, combinations of hydrated zinc oxide with hydrogen peroxide. The most reliable and efficient of these seems to be "ZPO special medicinal." This has the remarkable property of being fairly stable up to 140° C. and the manufacturers recommend that it be activated and sterilized by heating at that temperature for 4 hrs. We have found that loss of active oxygen under these circumstances is under 2%.

In applying any commercial material in therapy, we believe that excellent results can be obtained if the product that is employed is found by assay to be sufficiently active. Certainly before any attempt is made to use a given substance, it should be submitted to such an assay. ZPO special medicinal, even after sterilization as directed, gives a value of 6.7% to 7.0% of available oxygen, 10% to 12% of carbonate and 61% to 65% of total zinc. The loss in activity in storage appears to be about 1% per month.

For application the material is best made into an aqueous suspension, the consistency of which may

vary in accordance with the condition in which it is to be used. For example, in infections of the oral cavity it may be made into a very thin suspension and used as a mouth wash or gargle, while in wounds it is generally made into a 40% cream or paste, either packed into the recess or applied on sterile gauze.

One of the chief objections to using the material in the past has been the caking of such preparations after an hour or so. After some experimentation we found that this could be almost entirely overcome by incorporating 10% to 15% of sorbitol, or the less efficient mannitol. Suspensions made with sorbitol and 50% ZPO will not cake within 24 hrs. The preparation we recommend is as follows:

Zinc peroxide.....	40
Sorbitol.....	15
Tragacanth.....	1
Ringer's solution, <i>q. s.</i>	100

A good substitute can be made by using water in place of Ringer's solution.

Such preparations have been used under our observation in four cases of chronic undermining varicose ulcers with probable anaerobic infection. Although two of them were of long standing, all four ulcers showed marked healing, the pain was much reduced and the prognosis at present writing is very favorable. The peroxide preparation has been used continuously, being replaced by a new dressing every 24 hrs., and in no instance has any caking been observed.

SUMMARY

1. No evidence could be found for the existence of a true zinc peroxide. The commercial articles all contain hydrogen and are probably combinations of zinc oxide and hydrogen peroxide.

2. The substance for medicinal use should be assayed for active oxygen and it should not be called zinc peroxide.

3. The caking of suspensions can be overcome by adding sorbitol or mannitol. Four cases of chronic ulcer were treated by such a preparation with excellent results.

REFERENCE

- (1) Thenard, L. J., *Ann. chim. phys.*, 2nd ser., 9 (1818), 55; *Mem. de l'acad. sci.*, 3 (1818), 429.