these large and dangerous doses do not induce contractions in the eighth-day postpartum uterus, in all mothers. While the number of cases studied by us is relatively small (15 cases) these large doses of the alkaloids were found effective only in about 30% of the cases.

We have found, however, that *some* fluid extracts of ergot prepared in accordance with U. S. P. method, were effective in doses corresponding to 3–4 g. of ergot. The activity of these extracts could of course not be due to the known alkaloids (the amounts of these alkaloids as assayed by us were too small to account for the activity), and we undertook the problem of the isolation of the principle responsible for the efficacy of oral ergot dosage. While preparations containing 60–80% of this principle were obtained by us over a year and one-half ago, the isolation of the pure crystalline substance was made only Dec. 12, 1934. We have called this principle ergotocin. In human mothers this substance is uniformly effective when administered orally in doses of 0.3 mg. and intravenously in doses as low as 0.1 mg. The yield of 0.3 mg. of ergotocin is roughly equal to 3–4 g. of crude defatted ergot. This principle thus accounts for the activity of the fluid extracts.

Ergotocin has now been used on over 150 patients and no unpleasant symptoms have been observed with it. It controls uterine hemorrhage instantly. Intravenously the effect is noticed within fifteen seconds after administration. In the first stages the action of ergotocin resembles that of pituitary extracts, except that its effect lasts for three or four hours, in marked contrast to the transient effect usually obtained with pituitary extract. In its low toxicity, small dosage, prompt action in uterine hemorrhage, prolonged effect on the uterine muscles, ergotocin is unique among oxytocic principles.

Ergotocin salts, as well as the free base, are white, well-defined crystalline substances. The base melts with decomposition at 155°. The picrate, which is red, melts at 195–197°, with decomposition. When heated with alkali, ergotocin (or its salts) does not liberate any ammonia. Under the same experimental conditions, however, the known alkaloids (ergotoxine, ergotamine, sensibamine) eliminate quantitatively one mole of ammonia. The free base is somewhat soluble in water, and the salts are readily soluble. One may obtain even a 10% aqueous solution of some salts of ergotocin, a unique property among the alkaloids isolated from ergot. Ergotocin differs from the known ergot alkaloids (ergotoxine, ergotamine, sensibamine) in that it is not precipitated by Meyers' reagent in dilutions greater than 1 part in 7500, while the other alkaloids are precipitated in dilutions of 1:200,000 to 1:2,000,000. The optical rotation of the salts of ergotocin so far investigated is positive. The chemistry of ergotocin as well as some of the attempts to synthesize it will be reported as soon as the work now under way is complete.

We believe that with the isolation of this principle ergot therapy can now be put on a rational basis. If one bears in mind that many ergots do not contain this principle (and yet are acceptable on the basis of the U. S. P. assays), the cause of the difference of opinion among obstetricians regarding the value of ergot in obstetrics becomes evident.

The authors wish to take this opportunity to thank most sincerely the Research Corporation, Inc., for a grant which made this work possible and the Eli Lilly Co. for generously aiding us in this investigation.

Needless to say, without the coöperation and constant guidance of Drs. Davis, Adair and Rogers, on the clinical and pharmacological evaluation of this principle, this work would not have been brought to a successful conclusion.

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RECEIVED MARCH 30, 1935

THE SURFACE TENSION OF SOLUTIONS

Sir:

It has long been known that aqueous solutions of most salts have a slightly greater surface tension than water throughout the range of concentrations hitherto investigated and must, therefore, according to the Gibbs Theorem, be negatively adsorbed in the surface layer. According to Freundlich and earlier authors such "capillary inactive substances" give surface tension–concentration (σ–c) curves which are approximately straight lines with a gentle positive slope. Wagner [*Physik. Z.*, **25**, 47 (1924)] and later Onsager and Samaras [*J. Chem. Phys.*, **2**, 528 (1934)] have applied the Debye–Hückel theory of interionic attraction to the problem and derived an equation

$$\frac{\sigma}{\sigma_0} = 1 + \frac{79.517}{D\sigma_0}\, c \log \frac{1.143 \times 10^{-13}\,(DT)^3}{c}$$

for dilute aqueous solutions of all uni-univalent salts (D = dielectric constant; T = absolute temperature).

This equation predicts that the curve should be nearly straight in moderate concentrations, but that the limiting slope at extreme dilutions should be plus infinity.

We have devised a modification of the capillary rise method which has enabled us to measure the surface tension of solutions relative to that of water with greater precision than has hitherto been possible. The data for potassium chloride solutions are shown in the accompanying figure, together with a plot of the Onsager and Samaras equation. At extreme dilutions (less than 0.006 N) the surface tension is less than that of water, whereas above 0.006 N the surface tension is increased and is approximately a linear function of the concentration. These results are not in accord with the Onsager and Samaras equation, especially as to the sign of the limiting slope at extreme dilutions. Similar results have been obtained with potassium sulfate and cesium nitrate solutions. On the other hand, sucrose solutions from 0.0005 to 0.005 mole per liter, inclusive, when measured in the same apparatus, gave an increased surface tension. The effect which causes the diminution of surface tension and therefore, according to the Gibbs Theorem, also causes positive adsorption in the surface layer, is presumably due to an interaction between the polarized water molecules and the ions, which at extreme dilutions tends to force the ions into the surface layer. At higher concentrations the interionic forces predominate and cause negative adsorption and increased surface tension.

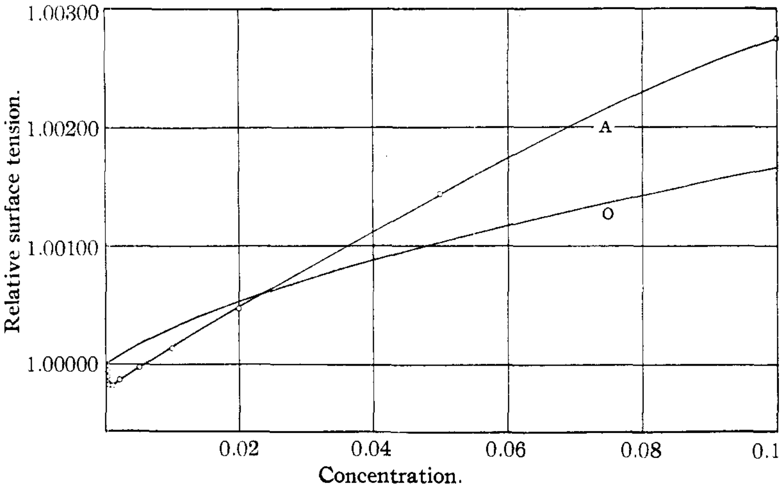

Fig. 1.—A, KCl at 25°; O, Onsager equation for uni-univalent salts.

The work is being continued both experimentally and theoretically to determine the general validity of the phenomenon and the factors which influence it.

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RECEIVED APRIL 18, 1935

THE MOLECULAR STRUCTURE OF GERMANIUM TETRACHLORIDE

Sir:

The electron diffraction investigation of the chlorides of the fourth group elements [L. Brockway and F. T. Wall, THIS JOURNAL, **56**, 2373 (1934)] has been extended by the study of germanium tetrachloride. Professor L. M. Dennis of Cornell University very kindly supplied a sample of the compound.

The photographs show two distinctive qualitative features: the little hump on the inner edge of the first strong maximum and the sloping shelf on the outside of the second maximum. Both of these characteristics appear in the theoretical intensity curve based upon a regular tetrahedral model included in Fig. 1 of the previous report. Two maxima were observed beyond the limit of the published curve.

The quantitative comparison is given in Table I. The third column gives the indicated values for the observed maxima and minima; the fourth gives the corresponding points on the theoretical curve and the fifth column shows the Ge–Cl interatomic distance. The first two points give values much lower than the average as has always been observed in the case of short distance (about ten centimeters) photographs of relatively large molecules [Ref. 1]. The value which Wierl [*Ann. Physik.*, [5] **8**, 548 (1931)] obtained with photographs covering only half of the present angular range is not altered by this more complete investigation.

Germanium tetrachloride shows about the same deviation (Table II) from additivity of the radii that the silicon and tin chlorides do. The sharp