The Vapor Pressure of Some Hydrates of Sulfathiazole Sodium*

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The sodium salt of sulfathiazole has been made available on the market in three modifications: namely, the anhydrous salt, the monohydrated salt and the sesquihydrated salt. The latter compound has been described by Christiansen (1), but published information concerning the other forms of sulfathiazole sodium is lacking. The experiments reported here were undertaken in order to determine which of the available forms of sulfathiazole sodium might be the most stable under ordinary conditions of temperature and humidity. Measurements of the water vapor pressure of the commercially available hydrates of sulfathiazole sodium were made at various temperatures and the data were correlated with determinations of moisture content. In addition, a crystalline hexahydrate of sulfathiazole sodium, isolated from an aqueous solution of the salt which was allowed to evaporate at room temperature, was identified and studied. Curves representing the variation of vapor pressure with change in temperature for the various hydrates and corresponding plots of the logarithm of pressure against the reciprocal of the absolute temperature were prepared and examined in relation to the stability of these salts.

EXPERIMENTAL

The vapor pressures of the hydrates of sulfathiazole sodium were determined in closed glass systems of approximately 15-cc. capacity. The respective hydrated salts, in amounts of from 1.0 to 2.0 Gm., were placed in appropriate glass bulbs, to each of which was attached a tube for evacuation and a short closed-end manometer filled with mercury. The air was then exhausted from each system by means of a mercury vapor pump, backed by a mechanical exhaust pump, until a minimum pressure that remained constant for 3 to 5 min. was established. Slight decomposition of the respective hydrates during the period of evacuation furnished sufficient water vapor to flush out residual air. The evacuated system was then sealed; the seal was allowed to cool; a millimeter scale was fastened to the manometer and the system was placed in a thermostatically controlled water bath which could be regulated to within 0.1° C. over the range of temperature employed.

Measurements of the vapor pressure were made at various temperatures from about 25° C. upward. The establishment of pressure equilibrium at each temperature was evidenced by the constancy and reproducibility of a given pressure reading. Since the pressure within the respective systems was found to respond readily to increase or decrease in temperature, it was possible to obtain equilibrium data by approaching equilibrium from both directions.

Moisture determinations were made by drying the respective hydrates in weighing bottles in vacuum over phosphorus pentoxide, and at 110° C. in an oven.

Measurement of the apparent transition temperature of the sesquihydrated to monohydrated salt was accomplished by means of a tensiometer of the Bremer–Frowein type using mercury as the manometric liquid.

The behavior of the various hydrates and of the anhydrous salt was studied under conditions which provided a temperature of 25° C. and a humidity which averaged 50%. Weighed portions of anhydrous, monohydrated, sesquihydrated and hexahydrated sulfathiazole sodium, contained in suitable tared weighing bottles, were exposed to those conditions. The bottles were weighed after 48 hrs. and after 10 days, the contents having been agitated by rotation of the containers from time to time during the period of exposure. Finally, the total moisture content was determined by drying at 110° C.

RESULTS

The results of vapor pressure measurements on commercially available monohydrated and sesquihydrated sulfathiazole sodium, and on the hexahydrated sulfathiazole sodium prepared in this laboratory, are shown graphically by the curved lines in Fig. 1.

The curve AB shows the reversible pressure changes with change in temperature obtained with commercially available sulfathiazole sodium monohydrate. When heated above 59° C., the commercially available monohydrate exhibited reversible aqueous tensions which lie on curve $A'B'CD$.

Curve EC shows the reversible pressure changes with change in temperature obtained with commercially available sulfathiazole sodium sesqui-

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hydrate. It may be noted that this curve intersects curve *A'B'CD* at about 65° C. This point represents a transition from the sesquihydrated form to the monohydrated form. Data obtained with the sesquihydrated salt above 65° C. coincided with the upper portion of curve *A'B'CD*.

Curve *FD* illustrates the reversible change of pressure with change in temperature of the hexahydrated sulfathiazole sodium isolated in this laboratory. This curve intersects the curve representing the vapor pressure of the monohydrated form at about 75° C., indicating a transition from the hexahydrated form to the monohydrated form at that temperature.

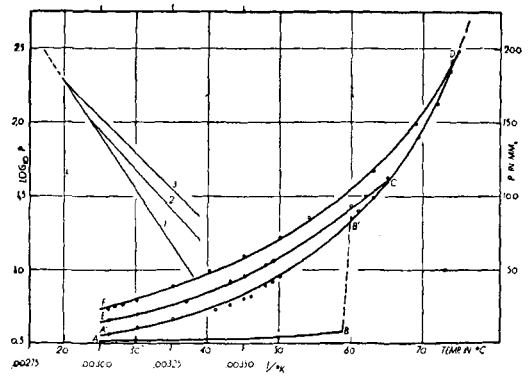

Fig. 1.—Vapor Pressure Curves for Sulfathiazole Sodium. Monohydrate (*AB* and *A'B'CD*), Sesquihydrate (*EC*), Hexahydrate (*FD*).

In Fig. 1 are also shown plots of the logarithms of the pressures in millimeters versus the reciprocals of the absolute temperatures. Within experimental error, the data presented by means of the vapor pressure curves yield straight lines representing the reversible monohydrate (line 1), the sesquihydrate (line 2) and the hexahydrate (line 3). The data of curve *AB* do not yield a straight line.

The phase changes indicated by the intersection of the curves plotted were confirmed by other observations. The hexahydrate melts incongruently under its own aqueous tension at about 75° C., while, by differential manometric measurement, the equilibrium pressure between the monohydrated salt and the sesquihydrated salt may be observed at about 65° C.

The moisture contents of the materials used, and the variation of moisture contents with time, under conditions which provided a temperature of 25° C., and an average humidity of 50%, are given in Table I.

TABLE I.—MOISTURE CONTENT MEASUREMENTS

	Theoretical	Found on Removal from the Original Container	Found at 25° C. and 50% Relative Humidity After 48 Hrs.	After 10 Days
Anhydrous	0.00	0.07	0.26	0.31
Monohydrate	6.10	5.10	5.23	7.60
Sesquihydrate	8.89	8.93	9.00	9.02
Hexahydrate	28.02	28.14	9.21	9.13

A number of specimens of the monohydrated salt yielded moisture contents closely approximating 5.1% as compared with the theoretical value of 6.1%. Such specimens changed slightly in 48 hrs. under the given conditions but the moisture content reached 7.6% in 10 days. Specimens of the sesquihydrated salt changed only slightly during the period of exposure, while specimens of the hexahydrated salt lost moisture rapidly during the 48-hr. period, approaching the sesquihydrate in composition. In marked contrast to the monohydrated and hexahydrated forms, the anhydrous material underwent practically negligible increase in moisture content during exposure to the same conditions.

With the exception of the somewhat low moisture content of the monohydrated sulfathiazole sodium, analyses of the various salts employed confirmed their composition.

SUMMARY

Commercially available sulfathiazole sodium monohydrate exhibits a low water vapor pressure over a range of temperature from 25° to 59° C. However, at about 59° C., the vapor pressure of the monohydrate undergoes a marked change. The break in the vapor pressure curve is assumed to represent an irreversible phase change. This behavior is suggestive of two structural modifications for the monohydrated salt of sulfathiazole sodium, since the salt absorbs water reversibly after having been heated above 59° C.

The vapor pressure of commercially available sulfathiazole sodium sesquihydrate is approximately 15 mm. at 25° C., and the compound exhibits transformation to the monohydrated form at about 65° C. The hexahydrate of sulfathiazole sodium has a vapor pressure of about 24 mm. at 25° C., and undergoes a transformation to the monohydrated form at about 75° C., evidenced by melting and recrystallization.

The commercially available monohydrate and the hexahydrate of sulfathiazole sodium appear to change to the sesquihydrate under conditions of 50% humidity at 25° C. The sesquihydrate of sulfathiazole sodium may therefore be considered to be the most stable hydrate of sulfathiazole sodium under average conditions. However, anhydrous sulfathiazole sodium resists absorption of moisture under these conditions.

REFERENCES

(1) Christiansen, W. G., *J. Am. Chem. Soc.*, 63 (1941), 632.