

quantitative method, we can state definitely that over 50% and perhaps all of the diethylphthalate is excreted by the kidneys.

A fairly accurate quantitative test was perfected for alcoholic solutions but not as yet for urine containing the diethylphthalate.

#### DISCUSSION AND CONCLUSIONS.

Diethylphthalate may be taken in considerable quantities (over 2 cc. per kilo of body weight per day) without causing any detectable damage. When injected intravenously into animals in doses of 0.25 cc. per kilogram it may cause death by paralysis of the respiratory center. It is rapidly excreted by the kidney. Doses that are insufficient to cause paralysis may cause convulsions due to an action on the central nervous system and which resemble somewhat the convulsions produced by strychnine. It seems probable, therefore, that if the function of the kidneys is below normal, sufficient diethylphthalate could accumulate in the blood to cause damage to the nervous system. In normal health, however, this seems improbable.

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### THE EFFECT OF BUFFERING THE OUTER PHASE UPON THE STABILITY OF CERTAIN EMULSIONS.\*

BY JOHN C. KRANTZ, JR.

#### INTRODUCTION.

The author with Gordon (1) studied the influence of changes of hydrogen-ion concentration upon the stability of cottonseed oil and mineral oil emulsions, when acacia and tragacanth were used as emulsifying agents. In another communication to THIS JOURNAL, the author (2) observed that acacia and tragacanth exerted a considerable amount of buffer activity upon the unbuffered outer phase of the emulsions. In this investigation, it was observed that with the emulsions in which acacia was the emulsifying agent, those emulsions having an unbuffered outer phase between  $p_H$  2.5 and 10.13 were buffered to approximately  $p_H$  4.3. Likewise those emulsions prepared with tragacanth, with unbuffered outer phases between these points of hydrogen-ion concentration, were buffered to approximately 5.5.

Considering thus the buffer capacities of the emulsifying agents, it becomes quite impossible to ascertain data from stability experiments for these emulsions when the outer phase was between  $p_H$  2.5 and 10.13.

In the previous investigations, using unbuffered solutions as the outer phase of the emulsions, the range of greatest stability with the emulsions prepared with acacia was between  $p_H$  2 and 10.5. Those prepared with tragacanth were most stable between  $p_H$  1.9 and 2.3. In view of the observations made on the buffering action of the emulsifying agent, in the previous experiments, the stability data did not actually include those ranges of hydrogen-ion concentration over which the emulsifying agent exerted its buffer capacity.

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\* Scientific Section, A. Ph. A., Rapid City meeting, 1929.

In order to ascertain stability data over this range of hydrogen-ion concentration, a series of emulsions was prepared buffering the external phase.

#### EXPERIMENTAL.

*Preparation of Universal Buffer.*—In order to make it unnecessary to vary the character of the buffer salts employed securing a large range of hydrogen-ion concentration, the universal buffer mixture of Prideaux and Ward (3) was employed. The buffer for this purpose was prepared by making a 0.2 *N* solution of the following acids, phenyl acetic, boric and phosphoric. The  $p_H$  of this primary buffer solution was 1.61. To obtain other values along the  $p_H$  scale, various quantities of 0.2 *N* sodium hydroxide solution were added.

Table I records the mixtures of acid and alkali, and the  $p_H$  of the resulting solution.

TABLE I.

No.	Primary acid buffer, cc.	0.2 <i>N</i> NaOH cc.	$p_H$ .	No.	Primary acid buffer, cc.	0.2 <i>N</i> NaOH, cc.	$p_H$ .
1	500	00	1.62	8	300	180	8.72
2	500	50	2.41	9	300	195	9.77
3	500	100	3.38	10	300	210	10.63
4	400	120	4.02	11	300	240	11.52
5	300	120	5.21	12	200	220	11.77
6	300	150	6.60	13	000	250	12.53
7	300	165	7.27			250 cc. H <sub>2</sub> O	.

*Emulsions with Acacia.*—Using the buffers described in the foregoing paragraphs as the external phase, two series of emulsions of mineral oil were prepared using acacia as the emulsifying agent. In each instance 40 cc. of a 25 per cent emulsion was prepared using 2.5 Gm. of acacia. The pharmaceutical method of triturating in a mortar was the procedure employed in the preparation.

Considerable change occurred in the  $p_H$  of the external phases after these had been used as the solvent for the gum. The results of these changes are recorded in Table II.

TABLE II.

No.	$p_H$ of outer phase.	$p_H$ of emulsion after 3 days.	$p_H$ of emulsion after 10 days.	No.	$p_H$ of outer phase.	$p_H$ of emulsion after 3 days.	$p_H$ of emulsion after 10 days.
1	1.61	2.78	3.00	8	8.72	6.92	6.91
2	2.41	3.30	3.37	9	9.77	7.13	6.99
3	3.38	3.73	3.73	10	10.63	7.75	7.13
4	4.02	4.08	4.16	11	11.52	8.73	8.05
5	5.21	4.93	4.95	12	11.77	11.27	11.24
6	6.60	5.73	5.70	13	12.53	12.10	12.07
7	7.27	5.93	6.02				

After a period of 10 days, equilibrium had undoubtedly established itself and there was no further appreciable change in hydrogen-ion concentration. Although on account of the comparative weak buffer capacity of the buffer solution employed, considerable changes were observed in the hydrogen-ion concentrations of the various emulsions, through these means it was possible to obtain several emulsions with varying points on the  $p_H$  scale on both sides of the neutral

point and study their stabilities. The stabilities of these emulsions were studied over a period of a hundred days. The emulsions prepared with 0.1 *N* sodium hydroxide solution  $p_H$  12.53 became quite yellow a few days after preparation, and then separated. The emulsions prepared with the buffer solution  $p_H$  11.77 were quite granular and separated into a inhomogeneous mixture with 4 to 8 days.

All of the other emulsions from  $p_H$  3.00 to  $p_H$  8.05 showed no variation in stability. The outer phases used in the preparation of these emulsions varied from  $p_H$  1.62 to 11.52.

*Emulsions with Tragacanth.*—Using the foregoing buffer solutions as the external phase, two series of emulsions of mineral oil were prepared using tragacanth as the emulsifying agent. In each instance 40 cc. of a 25 per cent emulsion was prepared using 0.5 Gm. of tragacanth. The pharmaceutical method of triturating in a mortar was the procedure employed in the preparation.

The hydrogen-ion concentrations of these emulsions was determined from time to time after preparation. After twelve days, when equilibrium was established, the following values were observed.

Table III records the changes in  $p_H$  which were observed in the outer phase after the preparation of the emulsion.

TABLE III.

No.	$p_H$ of outer phase.	$p_H$ of emulsion after equilibrium.	No.	$p_H$ of outer phase.	$p_H$ of emulsion after equilibrium.
1	1.61	2.09	8	8.72	6.45
2	2.41	2.84	9	9.77	6.89
3	3.38	3.44	10	10.63	6.93
4	4.02	4.05	11	11.52	9.31
5	5.21	5.21	12	11.77	11.63
6	6.60	6.20	13	12.38	12.34
7	7.27	6.33			

These data indicate that considerable change in hydrogen-ion concentration occurred in the outer phase buffer solution after the preparation of the emulsion.

Tables IV and V record the stability of two series of these emulsions over a period of 110 days.

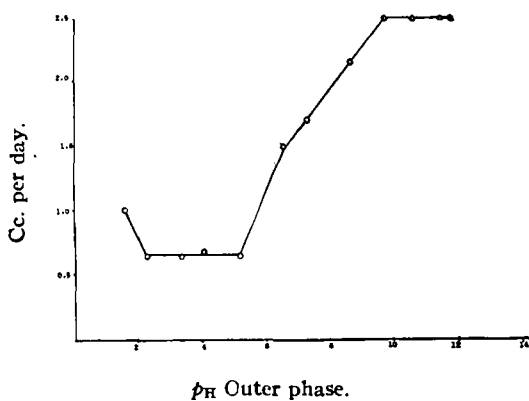
TABLE IV.—MINERAL OIL EMULSIFIED WITH TRAGACANTH.

No.	$p_H$ outer phase.	Degree of Separation in Cc. in Different Time Periods.								
		6	8	14	22	31	49	64	81	110
1	1.61	2	4	8	10	10	12	12	12	12
2	2.41			1	3	5	6	8	8	8
3	3.38			1	2	2	4	5	5	6
4	4.02			1	1	2	4	5	5	6
5	5.21			1	1	2	3	4	5	7
6	6.60					1	2	4	10	17
7	7.27						4	12	18	19
8	8.72				18	23	24	25	25	25
9	9.77				3	23	24	25	26	28
10	10.63					20	22	25	25	25
11	11.52				4	25	27	29	29	29
12	11.77				1	2	3	3	5	8
13	12.38	Slight yellow	Yellow 1 cc.	2	3	4	10	10	16	18

TABLE V.—MINERAL OIL EMULSIFIED WITH TRAGACANTH.

No.	$p_H$ outer phase.	Degree of Separation in Cc. in Different Time Periods.								
		Days.								
		5	7	15	21	30	48	63	80	111
1	1.61			2	5	5	8	9	9	9
2	2.41			1	1	2	4	5	5	6
3	3.38			1	2	4	5	6	7	7
4	4.02		1	4	6	8	9	10	10	10
5	5.21			3	4	5	7	7	7	7
6	6.60						2	5	10	15
7	7.27				3	7	12	18	18	19
8	8.72				18	20	22	22	25	25
9	9.77					11	26	26	28	28
10	10.63				1	20	26	27	27	28
11	11.52				18	22	26	27	27	28
12	11.77			2	2	2	2	3	5	8
13	12.38		Light yellow	Yellow	2	3	6	14	16	18

Omitting the data on emulsion No. 12 which was semi-solid and granular and those on No. 13 which contained no buffer salts in the outer phase, the stability data are plotted in graph No. 1.



Graph No. 1.

The ordinates of graph No. 1 represent the separation in cc. over a period of 110 days and multiplied by 10 to eliminate decimals.

The observations recorded indicate that the most stable range of hydrogen-ion concentration of these emulsions prepared with tragacanth lies within the  $p_H$  range 2.00 to 5.00. These findings with the buffered outer phase emulsions show a larger range of stability than the previous observations made by the

author and Gordon (1) when unbuffered solutions were used as the outer phase. In that series of investigations the most stable range of hydrogen-ion concentration of the outer phase with emulsions prepared with tragacanth was  $p_H$  1.9–2.3.

#### CONCLUSIONS.

(1) The stability of mineral oil emulsions with acacia and tragacanth, using buffered solutions as the outer phase, was studied at various hydrogen-ion concentrations.

(2) With acacia at various points along the hydrogen-ion scale from  $p_H$  2 to 10.5, no variation in stability was observed. As was observed previously those solutions more alkaline than  $p_H$  10.5 produced less stable emulsions.

(3) With tragacanth, the most stable range of hydrogen-ion concentration for emulsions, without a buffered outer phase is in the proximity of  $p_H$  2, with a buffered outer phase, the range extends from  $p_H$  2 to 5.

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LABORATORY OF PHARMACEUTICAL RESEARCH,  
SHARP AND DOHME.

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### THE LEAF OILS OF WASHINGTON CONIFERS: III. PINUS MONTICOLA.

BY ARNOLD J. LEHMAN AND E. V. LYNN.

This tree is commonly called western white pine. It is frequently 100 feet in height, with a straight trunk 4-5 feet in diameter and comparatively slender and spreading branches, which in young trees clothe the stem to the ground, forming a narrow, open pyramid. The symmetry is often broken in later years by the greater development of one or two of the upper branches. The young bark is thin, smooth and light green; on full grown trunks it is thick and has deep, longitudinal and cross fissures. The surface is covered with purplish scales, under which lies the cinnamon-red inner bark. The leaves, borne in clusters of five, are thick, rigid, blue-green and glaucous, 3 to 10 centimeters in length, and serrate, with small, minute teeth. In autumn the young cones are about two centimeters long but, when mature late the next summer, they are 12 to 25 centimeters long, shedding the seeds in early fall. The latter are about 8 millimeters long and colored a pale, red-brown, mottled with black.

Western white pines are scattered in considerable numbers throughout forests of the coast ranges and are not rare in the Cascades, where they occur at elevations of 5000 to 6000 feet. It reaches its noblest dimensions in northern Idaho, where it is found 2000 to 2500 feet above sea-level in river bottoms of streams flowing into Lake Pend Oreille. It is not, however, very abundant in Washington. The material for this work was gathered, partly in the spring and partly in the fall, from trees growing in a sphagnum-covered bog, well saturated with water, within a few miles of Seattle. The stand was quite abundant and consisted almost entirely of young trees, although a few older ones were found along the boundary of the swamp.

The leaves were separated as far as possible from the twigs and immediately distilled with steam. After roughly separating the oil, the aqueous distillate was once cohobated and the cohobated liquid was extracted with ether, which was then added to the oil. After carefully drying the ethereal solution, the solvent was largely removed by distillation, the last portions by means of a vacuum. The amount of oil thus obtained from 750 pounds was 180 cc., equivalent to 0.053 per cent.

The fresh oil had a pleasing, balsamic odor and was colorless, but became lemon-yellow on standing. The general constants were:  $d_{25}^{20}$  0.8695;  $n_D^{20}$  1.4724;  $[\alpha]_D^{25}$   $-17.31^\circ$ ; acid number 4.24; saponification value 26.78. Calculating the ester as bornyl acetate, the amount was 7.88 per cent, the quantity of alcohol from this 6.19 per cent.

The oil was first shaken with a 5 per cent solution of sodium carbonate to re-