next to the largest, the same preparation showed the smallest loss of alkaloids in that series. Light does not appear to have any particular effect on the alkaloidal content, but it appears to aid sedimentation. In all cases the ratio of alkaloids to total solids increased with time.

SUMMARY.

1. Ipecac preparations made by percolation with U. S. P. X and U. S. P. XI menstrua show little alkaloidal loss after sixteen months and deposit a small amount of sediment during the first two months after preparation.

2. Preparations made by percolation with acetic acid (9%) are not as stable as those prepared with hydro-alcoholic menstrua and should be prepared only for use in manufacturing processes.

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STABLE SUPERSATURATED SOLUTIONS OF CALCIUM GLUCONATE.[1]

BY GLENN L. JENKINS.

Various means have been developed to render supersaturated solutions of calcium gluconate stable. Heating in sealed ampuls (1) (2); the addition of alkali salts (3); the addition of boric acid or borax (4), (5), (6); the addition of aluminum chloride (7); the adjustment of the p_H of the finished product (8); and the addition of the soluble calcium salts of saccharic acid (9), mannonic acid (10) and lactobionic acid (11), (12) have all yielded products which have been used more or less in therapy. Numerous other compounds are reported in the references cited to produce some stabilization of supersaturated calcium gluconate solutions.

The observation that the calcium salt of methane disulfonic acid stabilized supersaturated calcium gluconate solutions led to the preparation and testing of a number of the soluble calcium salts of sulfonic acids. The salts prepared by heating the appropriate halide with an alkali sulfite and conversion of the product to the calcium salt included the calcium salt of: I, methane disulfonic acid (methionic acid) (13); II, ethyl sulfonic acid; III, ethane 1,1-disulfonic acid; IV, ethane 1,2-disulfonic acid; V, propane 1,2-disulfonic acid; VI, propane 1,2,3-trisulfonic acid and VII, benzene sulfonic acid (14). The average of two determinations of moisture at 180° C. and of two assays for calcium on the purified and dried salts are given in Table I.

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[1] Contribution from the Department of Pharmaceutical Chemistry of the College of Pharmacy of the University of Minnesota, June 15, 1937.

TABLE I.

	Compound.	Moisture %. Calc.	Found.	Calcium %. Calc.	Found.
I	$CH_2(SO_3)_2Ca.H_2O$	7.7	7.5	17.25	17.15
II	$(C_2H_5SO_3)_2Ca.2H_2O$	13.5	13.2	15.00	15.29
III	$C_2H_4(SO_3)_2Ca$	0.0	0.0	17.54	16.18
IV	$C_2H_4(SO_3)_2Ca$	0.0	0.0	17.54	17.32
V	$C_3H_7(SO_3)_2Ca.H_2O$	6.9	6.3	16.60	16.85
VI	$C_3H_5(SO_3)_3Ca_3.4H_2O$	9.6	9.8	15.78	15.61
VII	$(C_6H_5SO_3)_2Ca.H_2O$	4.8	4.5	11.30	11.14

The toxicity, hypercalcemia and irritant action of these salts compared to that of calcium gluconate, calcium lactate and calcium chloride were determined. The toxicity expressed as the minimum lethal dose in mg. per Kg. body weight was determined by intravenous injection into white mice. The irritant action and hypercalcemia were determined on dogs by intra-muscular injection in doses of 20 mg. of calcium per Kg. body weight, the volume of solution in each case being the same as for calcium gluconate and the blood calcium being determined at the end of one hour. The results are given in Table II.

TABLE II.

Compound.	Toxicity.	Increase in Blood Calcium, Mg. in 100 Cc.	Irritation.
Calcium gluconate	112.0	2.55	Slight
Calcium lactate	140.5	2.25	Marked
Calcium chloride	55.5	2.40	Severe
I	85.5	3.45	Slight
II	47.5	2.75	Severe
III	51.5	2.45	Severe
IV	68.0	2.80	Severe
V	53.0	2.60	Severe
VI	65.0	2.80	Slight
VII	50.0	2.30	Marked

The results indicate that calcium methionate is the best of the new compounds studied and that it is comparable to calcium gluconate as an agent for the increase of blood calcium. Calcium methionate having been found to be the best of the calcium salts of sulfonic acids studied, a further study of the value of this salt as a stabilizing agent for supersaturated calcium gluconate solutions was made.

The solutions were prepared by heating the required amounts of Merck's calcium gluconate which assayed 9.1 per cent calcium and calcium methionate which assayed 18.3 per cent calcium in sufficient water contained in calibrated flasks until solution occurred, replacing the water lost by evaporation, filtering through Jena No. 4 fritted glass and filling into soft glass bottles stoppered with rubber. Six bottles of each concentration of solution were prepared. Three of the bottles were kept in a room in which the temperature variations were approximately from 20° to 30° C. and three of the bottles were placed in a refrigerator which maintained a temperature of approximately 7° C. Observations of the solutions were made daily for 21 days and then at seven-day intervals for six months. The concentrations of the solutions and the time period during which two out of three samples deposited no crystals are given in Table III.

TABLE III.

Calcium Gluconate, Per Cent.	Calcium Methionate, Per Cent.	Days Stable, Room Temp.	Days Stable, 7° C.
5	1	200	200
5	3	200	200
5	5	200	200
7	8	200	200
10	5	11	14
10	10	200	193
10	12	200	200
10	15	200	63
10	20	200	182
10	30	200	175
15	5	7	0
15	10	8	1
15	15	49	56
15	20	119	77
20	10	2	0
20	20	35	8
20	30	17	28
25	30	28	6
30	35	3	1

Since one per cent of calcium methionate is equivalent to two per cent of calcium gluconate in calcium content, the data indicate that solutions which are stable and which contain an amount of calcium equivalent to from seven to seventy per cent of calcium gluconate can be prepared from the salts. Additional tests show that solutions prepared and sealed in ampuls are more stable than those in bottles. Solutions containing seven per cent of calcium gluconate and eight per cent of calcium methionate and solutions containing ten per cent of each salt when frozen in dry ice and allowed to thaw, yielded clear solutions. Other solutions of this concentration when agitated for five minutes each day for two hundred days showed no separation of crystals. Storage in amber bottles did not influence the stability of the solutions.

The stability of calcium gluconate-calcium methionate solutions does not appear to be influenced markedly by agitation, moderate changes in temperature or by light. Traces of extraneous matter which serve as centers of crystallization, such as sulfur from rubber stoppers, filter fiber, dust particles, and flaws in the glass of the bottle are the chief causes of instability.

SUMMARY AND CONCLUSIONS.

(1) Seven calcium salts of sulfonic acids have been prepared and tested for toxicity, production of hypercalcemia and irritation. It is shown that calcium methionate is the best of the salts studied.

(2) A study of the effect of calcium methionate in the stabilization of calcium-gluconate solutions has been made. It is found that solutions containing an amount of calcium methionate equal to or greater than the amount of calcium gluconate present yield relatively stable solutions containing the equivalent of from seven to seventy per cent of calcium gluconate.

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CONTROL OF SPECIALTIES AND NOSTRUMS IN PRESCRIPTION STOCK.*

BY JOHN F. MCCLOSKEY.[1]

Through the past centuries and up to the present time pharmacy has been confronted with many difficult and troublesome problems. Fortunately, when these problems are carefully considered and a clear understanding of the facts obtained, a solution is usually found; and when it is applied, generally the problem disappears and does not return, at least not in the same form.

The purpose of this paper is to present a very definite problem; one that is exceedingly complex and its ramifications are unbounded. Not only is the problem perplexing, but it has assumed the rôle of a profit-consuming Hercules. It demands attention and immediate action.

The title of this paper may indicate that the author has found a complete solution for the problem, but this is not so; the task is of such magnitude that it requires more than one brain and more than one solution. Nevertheless, definite suggestions are offered, mainly to promote discussion out of which may evolve some plan for control, as well as to guide those who may wish to follow them. I believe that if the suggestions were followed they would tend to lessen the severity and complexity of the problem.

The pharmacist has considerable difficulty in the control of his inventory relative to his prescription stock, mainly because once a preparation has been successfully introduced to the medical profession there follows an unlimited number of products that are similar, or, at best, just imitations of the original. Each of these products will have a group of followers made so by the extent of the advertising or the pressure of their salesmen. Naturally, it is expected that each of them will be stocked by the pharmacist.

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