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A COMPARATIVE STUDY OF THE ABSORBABILITY OF SIX CALCIUM COMPOUNDS.*[1]

BY A. RICHARD BLISS, JR., AND ROBERT W. MORRISON.

INTRODUCTION.

Two preliminary reports of this investigation have been published (1, 2). This paper reports the findings of the completed study, and covers the relatively wide gaps (0.25 mg.) between the quantities of Magnesium Sulphate required to completely neutralize the absorbed Calcium, presented in the previous papers, as well as time intervals above and below the time factor (2 hours) used in the earlier investigations.

The first study concerned itself with Dicalcium Phosphate, Calcium Chloride, Lactate, Glycerophosphate, Gluconate and Hexacalcium Inosite Hexaphosphate. These six calcium compounds and Calcium Lacto-phospho-gluconate were the agents investigated in the second study. The first six calcium combinations were employed in the final investigation.

Since a review of the literature related to these investigations has been included in the reports already published, space will be conserved by omitting the review in this final paper.

THE METHOD.

The technique (6) employed in the final study was the same as that used before, and is based on the antagonism between magnesium and calcium, earlier experiments having shown that animals narcotized by magnesium are awakened by injections of calcium salts, and, conversely, animals which have absorbed increasing quantities of calcium require greater amounts of magnesium for narcosis. Pure-bred albino mice were used. The calcium preparations were administered by stomach tube, and, after time intervals ranging from 30 minutes to 9 hours, magnesium sulphate was injected subcutaneously. Controls were run at the same time.

* Scientific Section, A. PH. A., Washington meeting, 1935.

[1] From The Reelfoot Lake Biological Station, Reelfoot Lake, Tennessee.

The mice received no water or food for from 12 to 15 hours before the ingestion of the calcium preparations. From 3 to 10 per cent aqueous solutions or suspensions of the calcium compounds were used. The magnesium sulphate was injected in the form of a 10 per cent aqueous solution. The index was the production of a definite degree of narcosis which presents itself with effective doses in from about 12 to 20 minutes after the injection of the magnesium sulphate solution. The required degree of narcosis was the point at which the mice lie on their backs without movement or attempts to turn over.

Extensive preliminary experiments demonstrated that 0.9 mg. of magnesium sulphate ($MgSO_4.7H_2O$) per Gm. of body weight is just adequate for the production of the required state of narcosis in albino mice. If some of the ingested calcium was absorbed, then a greater amount of magnesium sulphate is required to produce narcosis than is the case where no calcium is administered or absorbed. The amounts of each calcium compound administered in mg. per Gm. of body weight is equivalent to 0.3 mg. of calcium per Gm. of body weight. The tables following are self-explanatory.

Table I presents a summary of the results obtained in the studies already published.

TABLE I.—SUMMARY OF PRELIMINARY STUDIES.

Calcium Salt.	Amt. $MgSO_4.7H_2O$ Required for Partial Narcosis (Mg. per Gm.).	Amount $MgSO_4.7H_2O$ Required for Complete Narcosis (Mg. per Gm.).
Calcium chloride	1.25 (3 out of 3)	
		1.50 (3 out of 3)
Calcium lactate	1.00 (1 " " 3)	
	1.25 (3 " " 3)	
	1.50 (1 " " 3)	1.50 (2 " " 3)
		2.00 (3 " " 3)
Calcium gluconate	1.00 (3 " " 3)	
	1.25 (3 " " 3)	
	1.50 (1 " " 3)	1.50 (2 " " 3)
		2.00 (3 " " 3)
Dicalcium phosphate	1.00 (3 " " 3)	
	1.25 (1 " " 3)	1.25 (2 " " 3)
		1.50 (3 " " 3)
Calcium glycerophosphate	0.90 (2 " " 3)	
	1.00 (1 " " 3)	1.00 (2 " " 3)
		1.25 (3 " " 3)
		1.50 (3 " " 3)
Hexacalcium inosite hexaphosphate	1.00 (5 " " 5)	
	1.25 (4 " " 7)	1.25 (3 " " 7)
		1.50 (6 " " 6)

Since 0.9 mg. per Gm. of body weight is the minimum amount of magnesium sulphate ($MgSO_4.7H_2O$) required to produce the desired state of narcosis in albino mice which have received no water or food for from 12 to 15 hours, by subtracting 0.9 from the magnesium sulphate values given in the tables, the amounts of magnesium sulphate required to counteract the absorbed calcium are obtained; the larger the quantity of magnesium sulphate required for complete narcosis, the greater the amount of absorbed calcium.

Magnesium sulphate was administered in ascending doses of 0.25 mg. per Gm. in the preliminary studies. In the final investigation the dose was stepped up in 0.05 mg. per Gm. quantities so as to determine more closely and accurately the critical points. With each series determinations were made at 30-minute, 1-, 2-, 3-, 4-, 5-, 6-, 7-, 8- and 9-hour intervals after the administration of the calcium preparations. Each mouse was used for but one experiment.

One series of tables will suffice to show how the final studies were made and recorded. Tables II through IX give the results obtained with calcium chloride.

TABLE II.—CALCIUM CHLORIDE.

$MgSO_4$ injected 30 minutes after calcium ingestion.

Animal No.	Wt. (Gm.) of Mouse.	Dose of $CaCl_2$ (Mg. Ca per Gm. Body Wt.).	Dose $MgSO_4$ (Mg. per Gm. Body Wt.).	Minutes to Narcosis.
400	22.25	0.3	1.15	Partial, 20
401	12.20	"	"	" 22
402	13.64	"	"	" 17
403	19.55	"	1.20	" 22
404	24.48	"	"	" 20
405	20.19	"	"	Complete, 17
406	18.91	"	1.25	" 8
407	23.72	"	"	" 21
408	20.51	"	"	" 20

TABLE III.—CALCIUM CHLORIDE.

$MgSO_4$ injected 1 hour after calcium ingestion.

409	21.00	0.3	1.20	Partial, 23
410	12.22	"	"	" 21
411	21.77	"	"	" 20
412	25.55	"	1.25	" 25
413	20.20	"	"	" 24
414	25.12	"	"	" 20
415	20.37	"	1.30	Complete, 20
416	20.00	"	"	Partial, 12
417	12.80	"	"	Complete, 12
418	18.65	"	1.35	" 12
419	19.25	"	"	" 20
420	23.94	"	"	" 22

TABLE IV.—CALCIUM CHLORIDE.

$MgSO_4$ injected 2 hours after calcium ingestion.

421	15.77	0.3	1.25	Partial, 14
422	20.46	"	"	" 17
423	13.34	"	"	" 17
424	24.86	"	1.30	" 17
425	20.16	"	"	" 15
426	16.63	"	"	Complete, 14
427	24.61	"	1.35	Partial, 19
428	19.95	"	"	Complete, 17
429	15.32	"	"	" 10
430	20.00	"	1.40	" 8
431	15.30	"	"	" 5
432	27.20	"	"	" 12

TABLE V.—CALCIUM CHLORIDE.

$MgSO_4$ injected 3 hours after calcium ingestion.

433	20.00	0.3	1.25	Partial, 15
434	17.00	"	"	" 23
435	20.00	"	"	Complete, 11
436	17.00	"	1.30	Partial, 19
437	16.00	"	"	" 20
438	15.00	"	"	Complete, 9

439	13.56	"	1.35	Partial,	16
440	18.51	"	"	Complete,	10
441	21.09	"	"	"	7
442	20.32	"	1.40	"	10
				(Died, 15 min.)	
443	20.54	"	"	Complete,	10
444	20.41	"	"	"	8
				(Died, 16 min.)	

TABLE VI.—CALCIUM CHLORIDE.

$MgSO_4$ injected 4 hours after calcium ingestion.

445	21.83	0.3	1.30	Partial,	19
446	17.91	"	"	"	18
447	22.05	"	"	"	16
448	21.12	"	1.35	"	17
449	12.65	"	"	"	16
450	24.31	"	"	"	20
451	18.03	"	1.40	"	20
452	13.85	"	"	"	16
453	18.20	"	"	Complete,	8
454	16.79	"	1.45	"	14
455	21.23	"	"	"	20
456	22.36	"	"	"	13

TABLE VII.—CALCIUM CHLORIDE.

$MgSO_4$ injected 5 hours after calcium ingestion.

457	19.45	0.3	1.35	Partial,	16
458	15.32	"	"	"	17
459	19.87	"	"	"	17
460	27.85	"	1.40	Complete,	14
461	23.36	"	"	Partial,	16
462	17.41	"	"	"	19
463	15.30	"	1.45	"	19
464	18.45	"	"	Complete,	17
465	21.33	"	"	"	19
466	18.76	"	1.50	"	12
467	20.12	"	"	"	10
				(Died)	
468	14.85	"	"	Complete,	13

TABLE VIII.—CALCIUM CHLORIDE.

$MgSO_4$ injected 6 hours after calcium ingestion.

469	19.86	0.3	1.35	Partial,	21
470	19.23	"	"	"	14
471	24.76	"	"	"	18
472	27.54	"	1.40	"	16
473	22.27	"	"	Complete,	13
474	22.39	"	"	"	13
475	20.45	"	1.45	"	17
476	24.32	"	"	"	18
477	23.66	"	"	"	20

TABLE IX.—CALCIUM CHLORIDE.

$MgSO_4$ injected 7 hours after calcium ingestion.

478	17.50	0.3	1.30	Complete,	15
479	20.88	"	"	Partial,	15
480	21.75	"	"	"	13
481	18.45	"	1.35	Complete,	13
482	16.59	"	"	"	13
483	24.67	"	"	"	11

At the end of the 7th and 8th hours further uniform decreases in amounts of Magnesium Sulphate required for narcosis were observed. Table X summarizes the results obtained in the entire investigations through the seventh hour.

TABLE X.—SUMMARY OF COMPLETED STUDIES.

Magnesium sulphate required for complete narcosis at various intervals.

Drug.	30 Min.	1 Hr.	2 Hrs.	3 Hrs.	4 Hrs.	5 Hrs.	6 Hrs.	7 Hrs.
Calcium chloride	1.25	1.35	1.40	1.40	1.45	*1.50*	1.45	1.35
Calcium lactate	1.40	1.55	1.55	1.60	*1.65*	*1.65*	1.55	1.40
Calcium gluconate	1.30	1.30	1.35	1.45	*1.55*	1.50	1.45	1.40
Dicalcium phosphate	1.15	1.25	1.35	1.40	*1.45*	1.40	1.35	1.30
Calcium glycerophosphate	0.95	1.05	1.10	1.15	*1.25*	*1.25*	1.20	1.05
Hexacalcium inosite hexaphosphate	1.20	1.25	1.30	1.35	*1.45*	*1.45*	1.40	1.35

DISCUSSION.

The results obtained show that there is a fair degree of variation in the absorbability of the six calcium compounds studied. When arranged according to the maximum amount absorbed, they place themselves in the following order:

1. Calcium lactate.
2. Calcium gluconate.
3. Calcium chloride.
4. { Hexacalcium inosite hexaphosphate. / Dicalcium phosphate.
5. Calcium glycerophosphate.

With each compound there is a constant rise in the calcium absorbed until the fourth hour when a maximum absorption is reached for all of the calcium compounds studied excepting calcium chloride which requires five hours. The larger quantities of calcium are absorbed during the third, fourth, fifth and sixth hours after administration. The fall begins in the sixth hour.

It is interesting to note that the calcium-lactic acid combination heads the list. These observations are in agreement with the findings of McGowan and Bergheim. McGowan (3) demonstrated with rabbits that the most important single factor influencing the absorption of calcium and phosphorus seems to be the acidity of the gastric contents. Bergheim (4) has pointed out the significant influence the lactic acid radical has on the absorption of calcium, and suggested that the much higher proportion of lactose to calcium and phosphorus in human as compared with cow's milk may be a factor in the higher degree of utilization of the calcium content of the former. He attributes the fact to the production of a distinctly acid condition throughout the gastro-intestinal tract, due to increased lactic

acid formation in the intestine, Rowe and Kahn (5) having shown that the alkaline intestinal and pancreatic secretions and bile exert an inhibitory influence on the rate of calcium absorption.

It is obvious that of the six calcium compounds studied, in albino mice, calcium lactate is the most rapidly and effectively absorbed calcium compound for oral administration. It is reasonable to assume that the same may hold in human subjects.

The authors are indebted to Miss Jessie May Gill for valuable assistance during these studies in which over 900 albino mice were used.

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DRUGS AND BUGS.*

BY ERNST T. STUHR.[1]

The elemental forces which destroy and devour natural resources have long been interesting and fascinating to the curious mind. As the visible forces, such as floods, storms, famines and diseases, destroy progress in civilization, so too, are unnoticed destructive forces. Insects have long been known to be the most destructive of animals. Stored vegetable and animal products are subject to constant menace of invasion by parasites unless proper storing facilities and preventive precautions are observed.

The stock-room of the drug store is, in some instances, a disorderly, neglected and mistreated department of the store. If this is the case, a very untidy situation and atmosphere results, creating a haven for pest invasion of all kinds, including rodents (rats and mice), which are often carriers of bacteria and disease germs.

In general, drugs possessing an abundance of starch, inulin and sugars are most liable to the attack of pests. It should be kept in mind, however, that even in products not infested there is a gradual deterioration which in time renders many products unfit for use. Sanitary storage as a preventive measure is of importance in retarding deterioration.

Every retailer and wholesaler should be vitally interested and should profit by acquiring knowledge of the appearance and habits of the enemies which are harmful and detrimental to drugs in general. An acquaintance with the insect kingdom, as to harmful insect pests, their life cycles and habits and some of the possible preventive and combative means or methods, is essential. The ento-

* Scientific Section, A. PH. A., Washington meeting, 1934.

[1] Department of Pharmacology and Pharmacognosy, School of Pharmacy, Oregon State College.