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Drugs and Digestion.

BY

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DRUGS AND DIGESTION.*

By ROBERT G. ECCLES, M. D.

We smile at the incongruous prescriptions of last century, and wonder how either physicians or patients derived any satisfaction or benefit from them. We sneer at the young graduate who, in the confusion that arises from his new environment, writes orders for gross chemical or physiological incompatibles, and go from his office pondering upon the degeneracy of medical education. We never stop to question the wisdom of ourselves and others pouring into the stomachs of the sick in the most promiscuous manner, without regard to time or circumstances, drugs that inhibit or check the production of life- and health-giving peptone. In all chronic diseases the paramount consideration of every scientific medical man regards the patient's nutrition. Where we can not destroy pathogenic micro-organisms outright, the patient's only hope in the struggle for life lies in the strength of his cells, and their consequent power to triumph over their foes. High above every other consideration at such times is digestion. To interfere with or check it in the least, in many cases, is, then, criminal. When our remedies are incompatible with the gastric juice,

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the time of taking is likely to be of far more importance than the medicine itself. To weaken our patients by the production of artificial malnutrition gives their merciless diseases the advantage over them, where a little more knowledge would have enabled us to aid the vital forces instead of handicapping them. Important, therefore, as is the knowledge of the effects of drugs upon digestion, it has until the present year (1886) been almost totally neglected. Even in the administration of artificial ferments as aids to digestion the utmost recklessness prevails. Articles utterly valueless, with some of doubtful value, are, on the strength of advertisements and samples, used to the detriment of the sick. Prescriptions have been shown your essayist in various pharmacies in this city and New York for the compounding of which large prices were paid. The ingredients were the very best in the country, but the doctor's ignorance had rendered them totally worthless. First-class pepsin, one grain of which would digest one thousand grains of albumin in an hour, was in one case compounded with ingredients that rendered it utterly inert, and, on actual trial of a repetition of the same, it was found unable to digest a single grain in the same time. This physician probably condemned the pepsin for the bad results, as so many others, under similar circumstances, have done before and since.

Had such prescriptions been written by quacks or unknown practitioners, it would not have been a matter for grave comment. Being the work of men who stand high in the profession, it necessarily wore a more serious aspect.

Your essayist does not for a moment presume to think that laboratory experiments with flasks, bottles, or test-tubes can give exact physiological results. There are cases in which we know that the outcome of the internal use of certain drugs is apparently the very opposite of what might be

expected, reasoning exclusively from such data. Let the stomach be the seat of acetic or any other pathological fermentation, and the administration of powerful pepsin inhibitors, in not too large doses, will positively aid and hasten digestion. They exhaust their power in destroying a vicious ferment, and thus enable the otherwise inactive gastric juice to assume its function. Any alkali, alkaline carbonate, corrosive sublimate, carbolic acid, creasote, salicylic acid, or other powerful antagonist of pepsin, will here swing in as an apparent support of Hahnemann's dogma of similars curing similars. As we perceive the causes underlying such seeming contradictions, if we do not rest content with the groundless assumption that the stomach acts in some mysterious non-physical, non-chemical manner, we shall become masters of the situation. Its laws and those of the laboratory are the same, as far as they go together. Our reasoning is at fault when we fail to note the vastly greater complexity involving the one than the other. Whatever inhibits peptonization in the flask will do the same in the stomach, however much other things may mask it, or seem even to give reverse results. The lost power has only led to some unforeseen balancing gain. If we continue to wage war on the stomach's store of pepsin because we blundered into what proved a benefit at one or even two trials, we shall find that we are deceiving ourselves and damaging our patients. To give pepsin inhibitors when all has been gained that can be by compensation, or when no such compensation is possible, can lead only to ill. And yet this is being done daily and hourly in every civilized community upon the globe.

The study of the retarding effects of drugs upon digestion was first earnestly entered into by Dr. Klikovich, a Russian. The only brief notice of his work English-speaking people have had was given in the London "Lancet" on

June 19, 1886. The work embodied in this paper was begun in April of the present year. On September 4th the "Lancet" again informed its readers that O. Peterson, of St. Petersburg, had published the results of a similar investigation. These brief notices constitute all that is known upon the matter outside the Czar's dominions. The few drugs mentioned show in their results the bad effects of using dried albumin instead of fresh, and the effects of too large quantities of pepsin. Differences which to them seem to have been inappreciable, and that at the commencement of this work were thought impossible of procurement, have by experience been gained. Plan after plan was tried until the best was discovered. Many of the results were tested by from one to six repeated trials. All would have been so tested if another year could have been devoted to the work. Errors will creep in in spite of the utmost vigilance. For the first three months all the experiments were performed at a temperature of 38° to 40° C. (98° to 100° F.); but, for the purpose of saving time and expense and getting closer results, 49° C. was used. More than half of the old work was confirmed at the new temperature, so that they mutually proved each other. This was a compromise figure between the temperature of the stomach, 40° C., and that found in practice to be the quickest for artificial digestion, 55° C. When five grains of albumin were digested with one tenth of one per cent. of hydrochloric acid in water for one hour, using the same amount of pepsin each time, the following were the amounts undissolved at the temperatures given:

Degree Centigrade....	40°	44°	49°	55°	60°	66°
Albumin undissolved.	0·30	0·26	0·20	0·14	0·18	0·36

Other per cents. of acid were tried with corresponding results. A glance at the figures shows 55° C. to have the least undissolved albumin left. It would appear from this

that the failure of appetite in a patient is not due to the checking of digestion by fever. The products of such digestion, however, no doubt seriously affect the same. There are many kinds of peptone produced in peptic digestion. One of these, called by Meissner parapeptone (Reichert's "Foster's Physiology," page 965), is insoluble in neutral solutions. This is the one most abundantly produced at the higher temperature. Once formed, its further change into true peptone is impossible without the aid of trypsin. Could it be precipitated in the stomach, it would do no harm, since it would be carried through the pyloric orifice into the duodenum, there to complete its metabolism. Not being so precipitated, it finds in the stomach-walls a line of neutrality between the alkaline blood and the acid gastric juice, where it can be thrown down to check all osmosis. Like the dog in the manger, it will not form blood itself nor let that do so which could; consequently the patient must suffer. In cases where the fever does not produce such results, the doctor is kind enough to order it done on the advice of some advertising quack who patronizes his favorite medical journal. Artificially produced peptones of beef, eggs, or milk, prepared at all sorts of temperatures, are poured down the sick man's throat. It is in vain for him to proclaim that his stomach rebels and that he abhors the stuff—down it must go. It is in vain for him to say that his appetite is worse after it. That is reasoned away as due to the disease or to his having derived so much benefit from a former dose. There are peptones and peptones, and the quicker medical men know it the better. In all our digestion of albumin there would be a considerable amount of parapeptone produced but for the chloride of sodium taken with our food. During these experiments it was found that peptones produced in the presence of table salt could not be precipitated by neutralization. This was an important

discovery, and showed that the use of this article in our food has hitherto been partly misapprehended. To make alkali and acid for peptic and tryptic digestion it would have been as available, and it would seem even much more available, to take it with the water we drink. But we do not relish drinking salt water as we do eating salt meat or salt bread and butter. Wherever we relish salt, there without it parapeptone would be produced to block digestion. Wherever we do not relish it, there it could not avail in that direction. But salt delays digestion, so that an excess must be guarded against as injurious. When the amount of pepsin is made so small that it will require three hours and a half to digest the albumin used, the presence of one fifth of one per cent. of table salt in the total digestive fluid will delay it to double the time. Four fifths of one per cent. under the same conditions delay to seventeen hours.

Early in this investigation it was deemed advisable to determine whether acids other than lactic and hydrochloric could be used with pepsin to produce peptone. The generally accepted theory being that digestion is a hydrolytic change of the proteids, we should expect to find many other acids capable of producing this result. The following were

PER CENT. OF ACID.	1	0·8	0·6	0·5	0·3	0·2	0·1
	Grms.	Grms.	Grms.	Grms.	Grms.	Grms.	Grms.
Hydrochloric...	0·80	0·55	0·17	0·10	0·00	0·00	0·30
Phosphoric	0·00	0·05	0·12	0·26	0·71	0·93	2·36
Nitro-muriatic..	2·10	1·34	0·31	0·20	0·00	0·21	3·91
Lactic.....	0·35	1·31	1·89	2·16	3·19	3·90	4·15
Tartaric.....	0·39	1·29	1·82	1·96	3·08	3·75	3·93
Hydrobromic...	2·96	2·84	2·24	1·48	0·41	0·16	0·39
Nitric.....	2·27	1·93	1·57	1·41	0·60	0·71	1·89
Citric.....	1·47	2·22	2·50	2·71	3·73	3·92	4·06
Sulphuric.....	2·31	2·87	2·98	3·16	3·27	3·34	3·74
Hyperchloric ...	2·65	.....	.....	3·17	4·79	5·00	.....
Acetic	5·00	4·60	3·52	3·19	2·93	3·04	3·11
Hydrocyanic ...	.....	.....	5·00	5·00	4·87	4·01	.....

tried in the varying percentages marked in the first line of the table. The figures opposite the names of the acids represent the amount of albumin remaining undissolved at the end of the trial. The two that were not tried at every strength with the others were considered too doubtful to spend the time upon.

Hydrochloric acid was afterward tried with a reduced quantity of pepsin, and found to be most efficient at 0·2 per cent. It takes five times as much phosphoric acid to produce the same result as this small quantity of muriatic, while an increased or decreased quantity of muriatic only hinders. A small amount of phosphoric acid added to 0·2 muriatic improves digestion. This is the secret of acid phosphate becoming so popular, and of the efficiency of dilute phosphoric acid in dyspepsia. This, however, is not true of other acids, nor of this one above one per cent. or below one half of one per cent. The next table gives a list of the acids tried. Here digestion was completed in all, and time made the gauge instead of the amount of undissolved albumin. Fifteen centigrammes of absolute acid or its equivalent of dilute acid were added to the fifty grammes of solution. The first nine failed to come out in ten hours.

ACIDS.

1. Chromic acid	= over 10 hrs.	13. Tannic acid	= 3 hrs.
2. Picric acid	= " " "	14. Benzoic acid	= 2 h. 40 m.
3. Molybdenic acid	= " " "	15. Oxalic acid	= 2 h. 40 m.
4. Sulphuric acid	= " " "	16. Citric acid	= 2 h. 40 m.
5. Thymic acid	= " " "	17. Tartaric acid	= 2 h. 30 m.
6. Hydrobromic a.	= " " "	18. Oleic acid	= 2 h. 20 m.
7. Salicylic acid	= " " "	19. Boric acid	= 2 h. 15 m
8. Pyrogallic acid	= " " "	20. Acetic acid	= 2 h. 15 m.
9. Nitric acid	= " " "	21. Lactic acid	= 2 h. 15 m.
10. Hyperchloric acid	= 3 h. 40 m.	22. Phosphoric acid	= 2 h.
11. Cathartinic acid	= 3 h. 40 m.	23. Arsenious acid	= 2 h.
12. Chrysophanic acid	= 3 h. 40 m.	24. Gallic acid	= 2 h.

The test experiment in this set was over in two hours, so that the last three caused no delay. The last two owe their non-interference in all likelihood to their insolubility. They were practically absent. Benzoic acid did not inhibit as much as it was expected to, for reasons to be mentioned farther on. The nine that caused a delay of over ten hours were tried again after reducing to one third the former strength. This made them one part in a thousand of the solution. The next table gives the new results with the five centigrammes. The test time was again two hours.

Acids.

1. Chromic acid	= over 10 hrs.	6. Hydrobromic a.	= 3 h. 50 m.
2. Picric acid	= " " "	7. Salicylic acid	= 3 h. 20 m.
3. Molybdenic acid	= " " "	8. Nitric acid	= 3 h. 20 m.
4. Thymic acid	= 7 h. 40 m.	9. Carbolic acid	= 3 h. 10 m.
5. Sulphuric acid	= 5 h. 10 m.	10. Pyrogallic acid	= 2 h. 5 m.

As three again went over ten hours, at the next trial they were reduced again, one centigramme only being used, or one part in five thousand. The test time, by increasing the pepsin double, was reduced to one hour. Chromic acid came out in four hours and forty minutes, picric in four hours and a half, and molybdenic about the same. To make their effects non-appreciable would require their dilution to not less than one part in thirty thousand. Picric acid in contact with ground albumin over night causes a very marked shrinkage in the volume, so that it appears as if the larger bulk of it had been digested without pepsin. The following alkaloids and their salts were next tried. The test time was again two hours. Three parts in one thousand were used, or fifteen centigrammes in fifty grammes. The first on the list, ferrocyanide of quinine, was completely decomposed at the expense of the acid, and, although 0·4 per cent., or double the usual quantity, was used, its long delay was probably due to this. At the end of the experi-

ment, considerable Prussian blue had taken the place of the now dissolved chloride of quinine.

ALKALOIDS AND THEIR SALTS.

1. Ferrocyanide of quinine	= 5 h. 30 m.
2. Citrate of iron and strychnine	= 5 h. 20 m.
3. " " " " quinine	= 5 h. 10 m.
4. Sulphate of cinchonidine	= 4 h. 30 m.
5. " " cinchonine	= 4 h. 20 m.
6. " " quinidine	= 4 h. 20 m.
7. " " quinine	= 4 h. 10 m.
8. Bisulphate of quinine	= 4 h.
9. Sulphate of strychnine	= 4 h.
10. " " morphine	= 3 h. 40 m.
11. Tannate of quinine	= 3 h. 20 m.
12. Salicylate of quinine	= 3 h. 20 m.
13. " " cinchonidine	= 3 h. 10 m.
14. Chloride of quinine	= 3 h. 05 m.
15. Bromide of quinine	= 3 h.
16. Sulphate of atropine	= 3 h.
17. Hydrochloride of cocaine	= 2 h. 50 m.
18. Chloride of morphine	= 2 h. 45 m.
19. Bromide of caffeine	= 2 h. 40 m.
20. Veratrine	= 2 h. 40 m.
21. Strychnine	= 2 h. 30 m.
22. Aconitine	= 2 h. 20 m.
23. Brucine	= 2 h. 20 m.
24. Morphine	= 2 h. 15 m.
25. Acetate of strychnine	= 2 h. 15 m.
26. Chloride of pilocarpine	= 2 h. 15 m.
27. Acetate of morphine	= 2 h. 05 m.
28. Codeine	= 2 h.

The last one coming out evenly with the test, showed that its presence had not retarded any. It was again tried in double the proportion—*i. e.*, three centigrammes in fifty grammes. This time it did not come out for two hours and forty minutes.

In testing the essential oils found in the next table,

fifteen centigrammes were first dissolved in two grammes of alcohol and then added to the digesting fluid. Besides the usual control containing no drug, an extra one was added containing the same amount of alcohol as was used to dissolve the oil. This came out in two hours and ten minutes. The delay time of two grammes of alcohol was therefore ten minutes.

ESSENTIAL OILS.

1. Cinnamon	= over 10 hrs.	22. Wormwood	= 3 h. 10 m.
2. Pimento	= " " "	23. Erigeron	= 3 h. 10 m.
3. Lemon-grass	= " " "	24. Cajeput	= 3 h. 10 m.
4. Bitter-almond	= " " "	25. Rosemary	= 3 h. 10 m.
5. Clove	= 9 h. 50 m.	26. Nutmeg	= 3 h.
6. Bay	= 8 h. 40 m.	27. Rose-geranium	= 3 h.
7. Bergamot	= 8 h. 40 m.	28. Orange	= 3 h.
8. Sassafras	= 8 h. 20 m.	29. Lemon	= 2 h. 55 m.
9. Wintergreen	= 5 h. 10 m.	30. Wine (ethereal)	= 2 h. 50 m.
10. Rose	= 4 h. 50 m.	31. Amber	= 2 h. 50 m.
11. Origanum	= 4 h. 20 m.	32. Neroli (petale)	= 2 h. 50 m.
12. Citronella	= 3 h. 30 m.	33. Black-pepper	= 2 h. 50 m.
13. Caraway	= 3 h. 20 m.	34. Juniper	= 2 h. 40 m.
14. Coriander	= 3 h. 20 m.	35. Savin	= 2 h. 40 m.
15. Spearmint	= 3 h. 15 m.	36. Cedar	= 2 h. 40 m.
16. Pennyroyal	= 3 h. 15 m.	37. Patchouli	= 2 h. 40 m.
17. Aniseed	= 3 h. 15 m.	38. Croton	= 2 h. 20 m.
18. Fennel	= 3 h. 15 m.	39. Sandal-wood	= 2 h. 10 m.
19. Lavender	= 3 h. 10 m.	40. Cubeb	= 2 h. 10 m.
20. Peppermint	= 3 h. 10 m.	41. Turpentine	= 2 h. 10 m.
21. Thyme	= 3 h. 10 m.		

The first four were again tried with one third the amount of essential oil. Bitter almond then came out in three hours, and the others in five hours. A glance over the table shows that essential oils of similar origin, or derived from the same natural orders of plants, produce, as a rule, results very nearly alike. This is exemplified by the labiates spearmint, pennyroyal, lavender, peppermint, and thyme. The close relationship of cedar, savin, and juniper,

and also of fennel, coriander, and caraway, tell the same story for the families to which they belong. It is also somewhat singular to find the three oils of sandal-wood, cubeb, and turpentine as closely related here as they are in their physiological indications, although belonging to quite remote orders. Four balsams were, like the essential oils, dissolved in two grammes of alcohol and then added to the digestive fluid with the following results. The Canada balsam dissolved very imperfectly, so that its result is probably short of the true figure:

BALSAMS.

1. Tolu	= 5 h. 30 m.	3. Canada	= 2 h. 55 m.
2. Peru	= 4 h. 20 m.	4. Copaiba	= 2 h. 40 m.

In a former paper upon peptonization your essayist declared that the tinctures tried up to that time seemed to retard no more than the alcohol they contained. This has since proved to be a grave mistake. Only a few had been tried, and they under the influence of comparatively large quantities of pepsin. Up to that time, too, the method had been to digest a given time and weigh the remaining albumin. This plan was subject to such grave perturbations that it was finally abandoned for the better one of completing the digestion and taking the time consumed as a standard. A large number of tinctures were submitted to this method with the following results. The control time was again two hours. One gramme of each was added to the fifty grammes of fluid:

TINCTURES.

1. Chloride of iron	= over 10 h.	6. Lupulin	= over 10 h.
2. Iodine co.	= " " "	7. Belladonna	= 9 h. 05 m.
3. Chloride of iron (tasteless)	= " " "	8. Warburg's	= 8 h. 50 m.
		9. Cannabis ind.	= 8 h. 50 m.
4. Guaiaci	= " " "	10. Opium	= 8 h. 15 m.
5. Guaiaci ammon.	= " " "	11. Benzoin co.	= 6 h. 45 m.

12. Benzoin simp.	= 6 h. 10 m.	44. Krameria	= 3 h.
13. Verat. virid.	= 5 h. 30 m.	45. Quassia	= 3 h.
14. Cubeb	= 5 h. 30 m.	46. Valerian	= 3 h.
15. Buchu	= 5 h. 30 m.	47. Aloes	= 3 h.
16. Aloes and myrrh	= 5 h. 30 m.	48. Colchicum seed	= 3 h.
17. Valer. of ammon.	= 5 h. 30 m.	49. Cinchona co.	= 3 h.
18. Hyoscyamus	= 5 h. 20 m.	50. Stramonium	= 2 h. 55 m.
19. Asafœtida	= 4 h. 45 m.	51. Cardam. simp.	= 2 h. 45 m.
20. Tolu	= 4 h. 45 m.	52. " co.	= 2 h. 45 m.
21. Kino	= 4 h. 10 m.	53. Lobelia	= 2 h. 45 m.
22. Myrrh	= 4 h.	54. Squills	= 2 h. 45 m.
23. Catechu	= 3 h. 45 m.	55. Rhubarb co.	= 2 h. 45 m.
24. Colchicum root	= 3 h. 35 m.	56. Cinnamon	= 2 h. 45 m.
25. Digitalis	= 3 h. 35 m.	57. Ginger	= 2 h. 40 m.
26. Physostigma	= 3 h. 35 m.	58. Cantharides	= 2 h. 40 m.
27. Colocynth co.	= 3 h. 30 m.	59. Lavender	= 2 h. 40 m.
28. Modif'd Warb'rg	= 3 h. 30 m.	60. Ipecac co.	= 2 h. 30 m.
29. Avena sativa	= 3 h. 30 m.	61. Poke	= 2 h. 30 m.
30. Santal.	= 3 h. 30 m.	62. Rhubarb	= 2 h. 30 m.
31. Gentian co.	= 3 h. 30 m.	63. Aconite root	= 2 h. 30 m.
32. Sanguinaria	= 3 h. 30 m.	64. " leaf	= 2 h. 30 m.
33. Cinchona simp.	= 3 h. 30 m.	65. Lemon-peel(fr'sh)	= 2 h. 25 m.
34. Nux vomica	= 3 h. 20 m.	66. Opium, campho-rated	= 2 h. 20 m.
35. Cascarilla	= 3 h. 20 m.	67. Colombo	= 2 h. 15 m.
36. Senega	= 3 h. 20 m.	68. Angustura	= 2 h. 10 m.
37. Capsicum	= 3 h. 10 m.	69. Cochineal	= 2 h. 10 m.
38. Hops	= 3 h.	70. Virg. snakeroot	= 2 h. 10 m.
39. Gentian	= 3 h.	71. Conium	= 2 h. 10 m.
40. Orange-peel	= 3 h.	72. Arnica	= 2 h. 10 m.
41. Galls	= 3 h.	73. Dilute alcohol	= 2 h. 05 m.
42. Senna	= 3 h.		
43. Lobelia æther.	= 3 h.		

On another trial with half a gramme each of those that failed to complete digestion in the ten hours, the following results were had:

1. Tincture of	chloride of iron	= over 10 hrs.
2. "	iodine co.	= 9 h. 35 m.
3. "	chlor. iron (tasteless)	= 6 h. 50 m.

4. Tincture of guaiaci	= 6 h. 10 m.
5. " " ammon.	= 6 h. 10 m.
6. " lupulin	= 5 h. 50 m.

Tincture of the chloride of iron did not show just how thoroughly it retarded until the quantity was cut down to two centigrammes, or one part in two thousand five hundred. Here, then, is the worst tincture in the whole list, and it turns out to be the very one that theory has led physicians to almost universally prescribe with meals. Fortunately, the usual dose is so small that it can do no great amount of harm. But why let it do any? Is it not just as well to administer it between meals and allow our pale, anæmic patients the advantage of strength from their food as well as a richer oxygen-supply in the blood? If we must give a tincture of iron with the meals, then we had better use Creuse's tasteless. Even it retards to an injurious extent, and would be better given between meals. Some of the tinctures that are rarely if ever administered internally have the least retarding effect.

The principal organic bodies used in medicine and surgery, and not related directly to those already given, constitute the next table. With every one of these, fifteen centigrammes was the amount used, and two hours constituted the control time.

ORGANIC SUBSTANCES.

1. Beta naphthol	= 4 h. 50 m.	10. Concent. sulph. ether	= 2 h. 15 m.
2. Santonin, with 2 grms. alcohol	= 4 h. 45 m.	11. Powdered gum arabic	= 2 h. 15 m.
3. Chloroform	= 4 h. 40 m.	12. Sweet spirits of niter	= 2 h. 15 m.
4. Menthol	= 3 h. 40 m.	13. Acetic ether	= 2 h. 15 m.
5. Nitrite of amyl	= 3 h. 30 m.	14. Benzole	= 2 h. 15 m.
6. Croton chloral	= 2 h. 45 m.	15. Salicin	= 2 h. 05 m.
7. Chloral hydrate	= 2 h. 40 m.	16. Ethyl alcohol	= 2 h.
8. Vanillin	= 2 h. 40 m.		
9. Antipyrine	= 2 h. 15 m.		

17. Methyl alcohol	= 2 h.	21. Cane sugar	= 2 h.
18. Paraldehyde	= 2 h.	22. Glycerin	= 2 h.
19. Urea	= 2 h.	23. Santonin without alcohol	= 2 h.
20. Milk sugar	= 2 h.		

The last eight all came out of the bath with the control experiment, thus showing that there was no retarding effect. No. 23, being insoluble, was corrected by No. 2, where it was put into solution with alcohol. With six of the other seven it took six trials to discover their retarding effect. Urea caused a delay of twenty minutes when raised to thirty centigrammes. Methyl alcohol with three grammes delayed digestion an hour and thirty minutes beyond the control time, paraldehyde with the same amount was ten minutes behind this, and ethyl alcohol half an hour still longer. When eight grammes of white sugar were added to the fifty grammes of digestive fluid, a delay of one hour and five minutes over the usual two hours occurred, and, when the same amount of sugar of milk was put in, it took twenty minutes more than this. It would almost seem from these results that every article used in medicine had some little retarding power that would reveal itself on using it in large enough percentage. White sugar had the least of any of those tried. Milk sugar, so commonly mixed with pepsin to form the saccharated, is of no earthly advantage in it, and is really an injury to its value. The same is true of glycerin, where it is to be put to use at once. Six grammes of glycerin in a fifty-gramme mixture retard half an hour beyond the control time. As an antiseptic to protect the pepsin from bacteria, its utility is unquestionable. Common or ethylic alcohol in half the amount delays twice as long, so that a wine of pepsin is not so scientific as a liquid pepsin, although it is not so bad as some investigators have tried to make us believe. The usual dose of wine of pepsin diluted with the contents of the stomach

after a meal will reduce the alcohol to considerably less than one per cent. When in this proportion, its effects are inappreciable, and besides this the alcohol must all rapidly leave the stomach and allow the pepsin to act unaffected. This is probably what occurs where people are in the habit of drinking beer or wine with their meals. After stimulating the peptic glands a little, it rapidly diffuses itself through the system, and, as it has no permanent ill effect upon the digestive ferment, that at once assumes its proper duties. Along with the organic compounds of the last table a trial was made of two compound cathartics and two "after-dinner" pills in separate bottles. They came out together fifteen minutes after the control bottle, showing that their effects upon the digestive fluid are but slight. What their presence in the stomach might do by producing slight nausea and inhibiting the action of the digestive glands is another question that can only be answered by experiments upon patients. Of the fluid extracts but fifteen were tried. All of these except rhubarb came out on the first trial, when one gramme was used. It afterward came out in five hours when reduced to half a gramme. Control time, two hours.

FLUID EXTRACTS.

1. Aconite	= 2 h. 20 m.	8. Digitalis	= 3 h. 20 m.
2. Valerian	= 2 h. 30 m.	9. Wild cherry	= 3 h. 30 m.
3. Taraxacum	= 2 h. 30 m.	10. Buchu	= 3 h. 30 m.
4. Licorice	= 2 h. 30 m.	11. Cascara sagrada	= 3 h. 30 m.
5. Gentian	= 2 h. 40 m.	12. Buckthorn	= 3 h. 30 m.
6. Ergot	= 2 h. 40 m.	13. Guarana	= 3 h. 50 m.
7. Colchicum root	= 3 h. 10 m.	14. Hyoscyamus	= 3 h. 50 m

The methods of manufacturing fluid extracts, the materials used, and other considerations with regard to age, storage, etc., have such influence upon them that it was deemed a waste of labor to spend much time upon them.

When samples from different makers were compared, the results varied so widely that all further investigation was discontinued for the time being. The Pharmacopœia does not undertake to control their composition beyond telling how they shall be made, and it is doubtful whether its directions are followed even in this. The different amounts of dry extract contained in two samples of the same kind from different makers cause a wide variation in this line of investigation fatal to accuracy. This is true to a less degree of tinctures.

Before proceeding to a consideration of the long list of inorganic compounds it will be well to now pause and study pepsin itself as an organic drug. During this investigation fifty pharmacies were visited and their proprietors or managers questioned regarding the kinds of pepsin dispensed when no particular brand was specified by the physician. The inquiry extended to both pure and saccharated. A universal complaint against the doctors seemed to obtain in almost every place. They said that as a rule medical men did not seem to know themselves what they wanted when ordering, as the vast majority of them never wrote whether they wanted pure or saccharated. Sometimes they judged that saccharated was intended because of the large quantity called for and the evident poverty of the patient. At other times they gave the pure because only a few grains were wanted. Now here was a serious consideration for the poor dyspeptic or the patient suffering from enteric trouble, to say nothing of the child with diphtheria or the man with cystic blood-clot. In any such case had a pure pepsin been dispensed, one grain of which would digest over six hundred grains of albumin in an hour, the effects would vary very considerably from that of another where a home-made saccharated was given, one grain of which would barely digest six grains of albumin in the same time. The one, you will

perceive, would be one hundred times as strong as the other. This is no mere fanciful supposition, but actually what probably does occur very often in this and other cities of the United States. To have the same prescriptions dispensed, varying one hundred-fold in two contiguous pharmacies, because of the doubtful way in which we write them, is no light matter. Let such things increase in frequency, and universal skepticism of all medical science must be the outcome. Little things like this tend even now to make pharmacists look upon many physicians with some degree of contempt. When ordering pepsin, be sure and tell whether pure or saccharated is desired, and do not forget that the average price of the former is five or six times that of the latter. Out of the fifty, eleven used saccharated of their own make, five choosing Jensen's to make it from, three Fairchild's, and one each Merck's, Witte's, and Dieck's. Most of them took one part of pepsin to nineteen parts of sugar of milk; but some made it one part to seven. The remaining thirty-nine distributed their patronage upon the following brands as the figures indicate:

1. Hawley's	12	6. Manlius Smith's	3
2. McKesson & Robbins's	5	7. Lazell, Daly & Co.'s	2
3. Armstrong's	4	8. Tarrant & Co.'s	2
4. Schieffelin's	4	9. Lehn & Fink's	2
5. Schaffer's	4	10. Royal	1

The record of choice on the pure pepsins was lost, but Jensen's led all the rest, taking over one third of the patronage. Fairchild's came next. The following were the brands used:

American.

1. Fairchild's Scale.
2. Fairchild's Powdered.
3. Parke, Davis & Co.'s Pure.
4. Brent, Goode & Co.'s Prorsi.
5. McKesson & Robbins's Concent.
6. Armstrong's Pure.
7. Kidder's Crust.
8. Kidder's Crust, Powdered.
9. North's Pure.

10. Frazer & Lee's Pure.
11. Jensen's Crystal.
12. Golden Scale.
13. Royal Pure.
14. Dieck's Pure.

German.

15. Witte's.
16. Finzelberg's.
17. Merck's Scale.
18. Merck's Powdered.

English.

19. Bullock & Co., Dr. Beal's.
20. Morson's Porci.

French.

21. Boudault's Acid.

The peptic power of all these brands varies so widely that, as there is no standard by which to gauge them apart, both physician and druggist must remain at the mercy of accident or chance unless some one takes time to carefully work out their comparative merits. The test of the United States Pharmacopœia is worse than useless. No two men can get any approach to the same results by following it. That of the British is better, but still deficient. No one can rub albumin through a sieve and get the same results twice. The worn-off brass and its oxidation products retard all peptic digestion. On carefully grinding up in a mortar at one time enough egg albumin from eggs that had been boiled ten minutes to supply five grammes to each of the brands named, and after making it so fine that when a small mass of it was shaken up in water and held before a bright light no piece was so large that it would not pass through a forty-mesh sieve, the amount named being placed in a two-ounce bottle with forty cubic centimetres of dilute hydrochloric acid containing 0·2 per cent. of absolute acid, when the amounts of pepsin opposite the numbers given were added, in a solution of ten cubic centimetres, 0·2 per cent. HCl, the bottles kept at a temperature of 48° C. to 50° C. for one hour in a water bath with a double partition keeping them from the metal in contact with the flame, and shaken every ten minutes, they all came out within five minutes of each other with the same small amount of insoluble matter in each. Many experiments were required

to find out these figures, and care had to be taken to see that air particles did not get entangled with the albumin to keep it floating; otherwise a delay would have occurred. In each case from ten to fifty times the amount of pepsin given was weighed off and dissolved in an accurately measured quantity of dilute acid, so that the ten cubic centimetres just contained the required amount. Some of the home-made saccharated samples were not managed thus, owing to the bulk required. In one instance it took nearly three grammes to do the work. With this we took twenty c. c., leaving thirty c. c. to put with the albumin before adding the pepsin. This was prepared from a German brand of powdered, and nineteen parts of sugar of milk were added to one of it. The druggist was perfectly innocent of any intentional wrong in dispensing this. He had used an article made by a firm whose reputation for good goods is world-wide. They are no doubt themselves unconscious of the horribly poor quality of the stuff they are sending out to their patrons. It was diluted according to the formula recommended by several manufacturers of such goods. Think of it, physicians, and beware of your pepsin prescriptions if you want any results from them. This make, too, is used all over Europe as well as America, although over there they may not dilute it to one twentieth its normal strength as is done here. The scale pepsin of the same manufacturer, although also very poor, is nearly twice as good as the powdered. It is without exception the prettiest looking pepsin in the market. The scales glisten like silver, and look so clean and nice that, if we judged by mere appearances, we should take it every time in preference to all others:

SACCHARATED PEPSINS.

1.	21⅔ milligrammes,	or 1 to 234	6.	44½ milligrammes,	or 1 to 112
2.	220 "	" 1 to 23	7.	174 "	" 1 to 29
3.	64½ "	" 1 to 78	8.	171½ "	" 1 to 30
4.	37½ "	" 1 to 135	9.	55 "	" 1 to 91
5.	29 "	" 1 to 172	10.	93½ "	" 1 to 5

The poorest of these is beyond the requirements of the Pharmacopœia. It only requires one part to dissolve fifty parts in six hours. Here we have nearly one half of it dissolved in one hour. In six hours it would dissolve fully double the required amount. But what a wide difference in the different brands! No. 1 is ten times as strong as No. 2. The home-made articles are all far below the lowest of these, and simply because the druggist is misled by the false representations of the advertisers in medical and pharmaceutical journals. No man can follow the directions given and make an average sample of *pepsinum saccharatum* like that found in the market already put up. An examination of the pure pepsins, like that of the saccharated and under identical conditions, all being tested at once, gave the following results:

PURE PEPSINS.

1.	10 milligrammes,	or	1 to 500	12.	25 milligrammes,	or	1 to 200
2.	10 3/10 "	"	1 to 486	13.	48 "	"	1 to 104
3.	10½ "	"	1 to 475	14.	45 "	"	1 to 111
4.	10 7/10 "	"	1 to 459	15.	11½ "	"	1 to 447
5.	11 "	"	1 to 454	16.	22 "	"	1 to 227
6.	12⅜ "	"	1 to 403	17.	80⅝ "	"	1 to 62
7.	18⅝ "	"	1 to 269	18.	143 "	"	1 to 35
8.	18¾ "	"	1 to 266	19.	8 "	"	1 to 625
9.	21⅝ "	"	1 to 234	20.	13 "	"	1 to 385
10.	21⅞ "	"	1 to 232	21.	20 "	"	1 to 250
11.	21¼ "	"	1 to 236				

It is highly probable that the same brand of pepsin will vary less or more, according to the quantity in the stomach of the animal at the time of death. The process of extraction will necessarily keep them from any wide variation, but there may be enough to reverse the positions of any two of nearly the same digestive power, if samples prepared at different times are used.

It will be observed that quite a number of these range

below the best of the saccharated, although sold at much higher prices. The best in the lot is No. 19. It is of London make, and costs the large amount of $4 an ounce, so that it is out of the reach of many patients. The poorest is No. 18, and is from Germany. It has already been referred to. The cheapest of all is No. 1 of the saccharated samples, and is made in our own city. Whoever specifies and receives it gets more peptic power for the price charged than he could of any of the rest. Although only purporting to be a saccharated pepsin, it exceeds in digestive power many of the more pretentious and dearer articles. Among those possessing a high digestive power, and that must be used when a concentrated effect is necessary, No. 1 of the pure pepsins is the best, unless your patients are rich enough to pay for the English one already referred to. It is the best American pepsin for high peptic power. There is a class of goods now on the market known as peptone pepsins. The best of this kind is No. 11. You see from the figures given that it is only a shade better than the best saccharated, although costing six times as much. The high price charged for it, combined with the vast amount of advertising done in its behalf in our medical journals, has caused it to take precedence of most others in the pharmacies of this city. Never prescribe a peptone pepsin unless you give more than double the amount of it you would of any good pure pepsin, and then, remember, your patients' pockets will suffer. Where you must have a solution of pepsin in water, then the peptone pepsin is the very thing needed. Its great solubility gives it an increased value. Five compound pepsins containing pancreatin were found upon the market, and tested as to their peptic power only. The investigation of trypsin was deferred to a future time. These all had trade names attached to them, as follows: Lactopeptine, maltopepsine, speptine, dyspepsyn, and

lactated pepsin. Their relative powers ranged as the names are here given. Such combinations can be of little worth to the physician. In the stomach, if the pepsin is of any value, the other ferments can not be, as they are likely to be themselves digested or altered. If the stomach fails to act, then in the alkaline duodenum pepsin is useless. Had time permitted, this matter would have been put to actual test. Another of the peptic ferments with a trade name is ingluvin. This is said to be prepared from the digesting part of the alimentary tract of chickens. As a digesting agent it is almost valueless, and can not convert its own weight of albumin into peptone in an hour. A long list of elixirs of pepsin and lactopeptine are upon the market and being pressed. None of them has the activity of a good wine of pepsin, and all those containing ammonio-citrate of bismuth are nearly worthless. Such a combination is only a delusion arising from the name bismuth. A soluble salt of bismuth can not be substituted for the insoluble ones when their value consists in the fact that they are insoluble. An elixir of pepsin under the name of digestylin is now being advertised by samples among physicians. Its digestive power is just one tenth that of Hawley's aromatic liquid pepsin.

We come now to the consideration of inorganic substances and their effects upon digestion. It is no doubt unnecessary to remind you of the fact that no peptic digestion is possible without some acid, and that therefore all alkalies, alkaline carbonates, and such forms of matter as are acted upon by hydrochloric acid, are contra-indicated when digestion is going on, and must never be prescribed with pepsin. To order bicarbonate of sodium and pepsin in the same prescription displays lamentable ignorance on the part of any physician, and yet it is frequently done. As well might you fasten two horses of equal strength back to

back, and, by whipping them up, expect work to be done, as to hope for any benefit to your patient from such a combination. If an excess of the sodium is given, and acetic fermentation is going on, of course the patient will experience an advantage from taking it, but he would have had still greater benefit if the pepsin had not been given with it. As an illustration of the retarding effect of a drug because of its consuming the acid, iron reduced by hydrogen will answer. This one was quite a surprise when first discovered, although it should not have been so, as the inference *a priori* of its action is simple. The longer the iron is kept in contact with the acid, the more it retards. If put to digesting at once, the addition of an extra supply of acid hastens the work. Fifteen centigrammes delayed digestion 390 minutes after the two hours of the control experiment were up. By raising the acid strength to 0·4 per cent., the same amount only delayed 210 minutes.

The following list is that of the worst retarders yet found. Only five milligrammes, or one part in ten thousand, were necessary to produce the delay mentioned. The control time is already subtracted in this and all subsequent tables. The time is given in minutes only:

	Minutes.		Minutes.
1. Molybdate of ammonium	190	4. Chloride of platinum	60
2. Molybdenate of sodium	180	5. Potassio-mercuric iodide	60
3. Permanganate of potass'm	130		

The next list comprises those that allowed digestion to finish after delaying the indicated time, when one centigramme, or one part in five thousand, was used. The two hours of control time are extracted:

	Minutes.		Minutes.
1. Ammonio-ferric alum	330	7. Sol. of perchloride of iron	50
2. Ferricyanide of potassium	320	8. Salicylate of lithium	30
3. Ferrocyanide of potassium	260	9. Chloride of gold	20
4. Sulphate of iron	130	10. Bichloride of mercury	15
5. Bichromate of potassium	130	11. Sulphate of sodium	15
6. Chromate of potassium	60	12. Sulphate of potassium	15

The following were tested from 150 up to 50 milligrammes, and when of the latter strength they delayed as follows:

	Minutes.		Minutes.
1. Ammonium sulphite	460	5. Mercuric nitrate	80
2. Magnesium sulphate	330	6. Cadmium iodide	50
3. Iron and potass. tart	290	7. Sodium hyposulphite	20
4. Antimony and potass. tart.	100		

The next long list is composed of such non-organic drugs as digested the submitted albumin in the time named, plus the two hours of control time, when fifteen centigrammes were added to the fifty grammes. The proportion was therefore three parts to one thousand.

	Minutes.		Minutes.
1. Chloride of ammonium	320	26. Benzoate of potassium	110
2. " " calcium	250	27. Sulphide of potassium	650
3. " " sodium	200	28. Sulphate of ammon. and alumin	750
4. " " antimony	160	29. Sulphate of copper	720
5. " " potassium	90	30. " " magnesium	690
6. " " lithium	60	31. Hypophosphite of manganese	80
7. Bromide of iron	360	32. Hypophosphite of sodium.	60
8. " " ammonium	200	33. Hypophosphite of potassium	40
9. " " lithium	120	34. Chlorate of sodium	280
10. " " sodium	100	35. " " potassium	200
11. " " cerium	90	36. Acetate of sodium	30
12. " " potassium	60	37. " " ammonium	30
13. Iodide of potassium	200	38. Sulphocarbolate of zinc	140
14. " " arsenic	190	39. " " sodium	80
15. " " sodium	180	40. Phosphate of iron	60
16. " " ammonium	170	41. " " sodium	30
17. " " lead	60	42. Salicylate of sodium	690
18. " " calcium	5	43. " " potassium	360
19. Nitrate of sodium	450	44. Valerianate of ammonium.	60
20. " " potassium	390	45. " " zinc	30
21. " " strontium	380	46. Ammon. citr. of iron	410
22. " " uranium	310	47. " " " bismuth	90
23. Benzoate of sodium	160		
24. " " ammonium	160		
25. " " lithium	140		

	Minutes.		Minutes.
48. Sulphite of sodium.....	330	52. Biborate of sodium.....	10
49. Citrate of iron, U. S.....	60	53. Arsenate of sodium.....	10
50. Oxalate of cerium.....	60	54. Cyanide of potassium	5
51. Lactophosphate of calcium	10		

A glance over this list shows that the sulphates are the most active inhibitors of digestion. Among the alkaloidal salts the same was the case. Why sulphate of quinine ever came to be so universally prescribed in preference to the much better chloride is hard to tell. The same is true of sulphate of morphine. In the chlorides there is more of the active principle to the same weight, they are much more soluble in the gastric juice, and they retard digestion less. Next to the sulphates the nitrates are the great retarders. The bromides average lower than the chlorides, while the latter are about even with the iodides. Bromide of iron ranges high, like many of the iron non-organic salts. Dialysed iron and the solution of pernitrate of iron retarded respectively 150 and 110 minutes when fifteen centigrammes were used, which is lower than the run of their class. The salicylates are far above the benzoates, and the chlorates hinder much more than the chlorides. The general run of all agrees very well with the activity of their acids, according to a preceding table. The next list comprises those having the least retarding power of any tried. When fifteen centigrammes were used, no effect could be perceived. The amount was therefore doubled, thus making three parts in five hundred.

1. Acetate of potassium	280	4. Tartrate of potassium.....	50
2. Citrate of potassium.....	90	5. Rochelle salts.....	20
3. Phosphate of calcium.....	60	6. Acetate of lead.....	5

It has been observed during this investigation that antiseptics averaged high as retarders, and an approach is made by them in this power that runs nearly parallel with their germ-destroying power. Potassio-mercuric iodide, the most

potent germicide known, was found to hold back digestion one hour when only one part in ten thousand was used. Bichloride of mercury required but one part in five thousand to retard fifteen minutes. While there are substances not known to be germicides that retard still more, still it is somewhat curious to find this class range so high, and at the same time occupying positions toward each other that suggest the order of their germ-destroying power. The molybdates seem to lead everything else as inhibitors, and they are the very best-known precipitants of peptone. Homœopathists should make some "provings" upon the salts of molybdenum, and use them as cures for dyspepsia. They would certainly have similar results from the drug as from the disease.

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