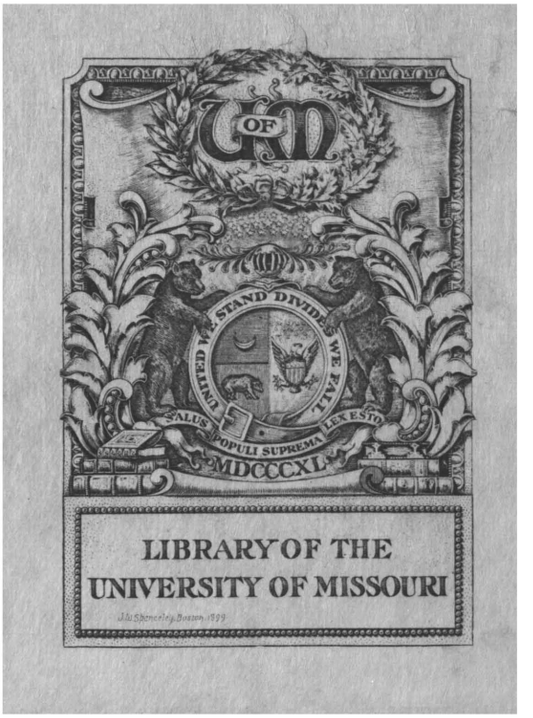
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"VARIATIONS IN THE AMYLOLYTIC POWER AND COMPOSITION OF THE SALIVA."

by

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"VARIATIONS in the AMYLOLYTIC POWER and COMPOSITION of the SALIVA."

INTRODUCTORY.

Investigations concerning the variations in the character of the human saliva have had to do for the most part with those variations of the amylolytic power and composition which occur under normal conditions, and of the adaptation of the saliva to diets specific in character. In animals, however, the field of investigation has naturally broadened out considerably, and the questions of amylolytic power and of the many variations occurring under different conditions in the composition of the saliva, have been much more fully investigated.

The effect of drugs upon the character of saliva, the amylolytic power especially, seems to have been almost entirely neglected. The well known effects of Atropine and Pilocarpine on the salivary glands, as regards quantity, should be extended to include the composition and digestive properties of the secretions as well.

In the present paper I shall present some results obtained from studying the variations in the amylolytic power and composition of the human saliva after administration of these drugs.

HISTORICAL.

Mechanism of Salivary Secretion:- The existence of secretory nerves was first discovered in 1851 by Ludwig,(1), who found that stimulation of the chorda tympani nerve caused a flow of saliva from the submaxillary gland.

The salivary glands receive a double nerve supply, on one hand from the medulla by way of cranial nerves, and on the other, fibres from the spinal cord through the cervical sympathetic. The cranial fibres to the submaxillary and sublingual glands are carried by the chorda tympani (from the facial and 5th), while those to the parotid pass through Jacobson's nerve from the 9th cranial. The sympathetic fibres arise from the cervical region of the spinal cord and are relayed to the glands via the superior cervical ganglion.

The greater number of secretory fibers are carried by the cranial nerves, being accompanied by vaso-dilators, while a smaller number of secretory fibers which seem to be connected especially with the secretion of the organic constituents of saliva, pass to the glands through the cervical sympathetic and are accompanied by vaso-constrictor fibers.(2)

To apply Heidenhein's (3) theory of secretory and trophic fibers, stimulation of the cranial fibers, then, would cause vaso-dilation and a secretion of water and inorganic salts, these fibers being the secretory nerves proper; while stimulation of the trophic or sympathetic fibers would cause vaso-constriction and the formation of the organic constituents within the cell,

ready to be carried out with the secretion of water.

Under normal conditions the flow of saliva from the salivary glands is the result of reflex stimulation of the secretory nerves, by way of the sensory fibers from the mouth and tongue. Sapid bodies and other chemical and mechanical stimuli when applied to the tongue or mucosa of the mouth will cause a flow of saliva, their effects being in the following descending order of strength: (1) acids, (2) neutral and alkaline salts, (3) bitter substances, and (4) sweet substances. (2) Such psychical acts as the thought of savory food and the feeling of nausea, will also cause a flow of saliva, the effect in this case probably being due to stimulation of the secretory centre by impulses from the higher centres. Lastly, the medullary centre may be inhibited as well as stimulated, the well known effect of fear, anxiety and embarrassment in producing a parched throat, being supposed to arise in this way by the inhibitory action of nerve impulses arising in cerebral centres.(4

Variations in Volume Secreted:- Variations in the volume of saliva secreted are the most noticable changes in the saliva which occur upon variation of the conditions of the secretion; the point and character of the direct stimulation, the character of the food, and the drugs employed, are important factors in regulating the quantity of saliva secreted. It is well known that stimulation of chorda tympani will cause an abundant flow of saliva; unless the chorda has been recently stimulated, excitation of the sympathetic fi bers causes practically no secretion at all. (5) By proper regulation it may also be shown (4) that the volume of saliva secreted increases with the strength of

the stimulus, provided the gland was previously in a resting condition.

The volume of the saliva is adapted to the varying mechanical needs occurring with the different character of the food. Scheunert and Gottschalk (6) in experimenting on the horse recently demonstrated that the volume of saliva secreted increases with the relative dryness of the food which is being masticated, and also that it decreases with the diminishing appetite as the end of a meal approaches. The following is taken from their tables:-

Food	Ex. 1. Volume	Ex. 11. Volume
Hay	190 c.c.	1304 c.c.
Dry Bread	176 "	218 "
Oats	157 "	330 "
Grass	147 "	
Fresh Bread	123 "	121 "
Potatoes	72 "	43 "
Turnips		23 "
Raw Potatoes		2 "

Scheurnert and Gottschalk (6).

Time in Minutes.	Vol. Saliva Food=1500 g. Hay	Vol. Saliva Food=3000 g. Oats.
1 - 5	190 c.c.	157 c.c.
6 - 10	186	150
11 - 15	162	114
16 - 20	150	111
21 - 25	146	89
26 - 30	143	107
31 - 35	149	76
36 - 40	131	55
41 - 45	125	31
46 - 50	124	55
51 - 55	151	31
56 - 60	104	14

Scheunert and Gottschalk (6).

Scheunert and Illing (7) also obtained similar results upon two horses.

The variations in volume caused by different chemical stimuli, acids, alkalis, etc, have already been referred to in the paragraph upon reflex saliva, but the effect of certain drugs is an important factor which remains yet to be considered. The experimental work upon this particular phase of the subject has been limited largely to the action of pilocarpine, atropine, and nicotine, and their effects are well known. Pilocarpine produces a profuse secretion in moderate doses, while very small doses of atropine will inhibit the secretion entirely, the current theory

being that the former stimulates and that the latter paralyzes the secretory nerve endings. (33) (34) Nicotine also prevents salivary secretion, but by the paralysis of the connections between the nerve fibers and the ganglion cells, through which they pass, and not by direct action upon the nerve endings oamong the gland cells. (8)

Bottazi, D'Errico, and Jappeli (9) recently showed that solutions of adrenalin will also cause a complete stoppage of the flow of saliva, no secretion occurring upon electrical stimulation of the secretory nerves after injection of the drug.

Variations in Composition:- Jappeli (10), in working upon the effect of the point of stimulation upon the saliva, obtained results showing that the solid content increases in the following order, 1 reflex or spontaneous saliva, 2 chorda (direct stimulation), 3 sympathetic saliva (direct stimulation). The fact that sympathetic saliva contains amuch higher percentage of organic solids than does chorda saliva has long been known, it being in fact the foundation upon which rests the theory of "trophic" and "secretory" fibers to the glands. There is one exception to this rule, however, Langley (11) having demonstrated the fact that in the cat the chorda instead of the sympathetic saliva is the more consentrated. As inthe case of the volume, the strength of the stimulus regulates the solid content of the saliva. (4) The salts and water increase with the stimulus up to about .77 per cent, while the increase in organic constituents depends upon the condition of the gland. If it is in a rested condition theyincrease along with the salts and water, but if the

gland is fatigued the increase is only temporary, and is followed by a fall.

Exper.	Saliva.	Organic Solids per 100 c.c.	Exper.	Saliva	Organic Solids per 100 c.c.
1.	1. Chorda	1.14	5.	1. Chorda	1.06
	2. Sympathetic	1.58		2. Sympathetic	1.96
2.	1. Chorda	.73	6.	1. Chorda	1.24
	2. Sympathetic	1.58		2. Sympathetic	1.29
3.	1. Chorda	.84	7.	1. Chorda	1.11
	2. Sympathetic	1.56		2. Sympathetic	2.40
4.	1. Chorda	.89	8.	1. Chorda	.71
	2. Sympathetic	1.49		2. Sympathetic	1.43

Carlson, Greer, Becht (14). Showing relative organic solid content of chorda and sympathetic saliva.

Heidenhain (12), after working upon dogs and rabbits, reported that there was no increase in solids upon diminishing the blood supply to the parotid gland, and concluded therefore, that the vascular condition (sympathetic, vaso-constriction and chorda vaso-dilation) of the gland was not a factor in determining the difference in the chorda and the sympathetic saliva. Heidenhain's theory of trophic and secretory nerves, therefore, has been largely depended upon to explain the difference in content of the chorda and sympathetic salivas. But there has recently been some opposition to this prevalent hypothesis.

Langley and Fletcher (13) in 1888 found that diminution of the oxygen supply by dyspnoea, as well as diminution of the arterial blood supply by partial bleeding, increases the percentage of solids in the dog saliva from the submaxillary gland. They thought that probably the s ympathetic saliva might be more

concentrated than the chorda saliva because of the diminished blood supply to the gland; they did not conclude that such was actually the case, in view of the fact that in the cat the chorda saliva is normally more dilute than the sympathetic.

Langley (38) in his work upon the action of atropine upon the secretory nerves, found that after atropine neither the organic constituents nor the salts of sympathetic saliva were increased by chorda stimulation. If the trophic fibers had escaped paralysis, there would have been a marked increase in the percentage of organic substance, such as Heidenhain obtained by stimulation of the sympathetic and Jacobson's nerve simultaneously. He stimulated for hours after atropine, but never saw insections of the heart and gland any indication of the formation of fresh substance, whereas without atropine, a distinct outer protein zone would have been found. Langley concluded, therefore, that the "anabolic" fibers were paralyzed at the same time as the "secretory" fibers, and the secretory fibers at the same time as the "trophic" fibers; or, in other words, the phenomena of atropine poisoning gives no indication of more than one kind of secretory fibers in the chorda.

Carlson, Greer, and Becht (14) have recently shown also that the variation of the oxygen supply of the submaxillary gland due to sympathetic, vaso-constriction or chorda vaso-dilation, is sufficient to account for the variation in the solid content of the two salivas. Even in the case of the cat diminished blood supply causes sympathetic saliva to be more concentrated than the normal chorda saliva. The following results obtained by

occlusion of the gland artery both on the dog and cat, illustrates Carlson's point:

No.of Ex.	Saliva-Submaxillary Gland.	Solids per 100 c.c. Total.	Inorganic.	Organic.
1. Dog	1. Sympathetic	1.91	.40	1.51
	2. Chorda	1.16	.40	.76
	3. " art. occluded	2.28	.50	1.78
	4. Chorda	1.13	.31	.82
2. Dog	1. Sympathetic	2.26	.59	1.67
	2. Chorda	1.10	.44	.66
	3. " art. occluded	2.31	.43	1.88
	4. Chorda	1.20	.31	.89
3. Dog	1. Reflex (Ether)	.89	.24	.65
	2. Sympathetic	1.23	.33	.90
	3. Chorda	1.32	.61	.71
	4. " partial art. occluded.	1.73	.77	.95
	5. " freater art. occluded.	2.03	.64	1.38
4. Cat	1. Chorda	.60	.13	.47
	2. Sym. art. compressed	.89	.16	.73
	3. " " "	.89	.24	.65
	4. " great vaso-constriction.	1.03	.27	.76
	5. Chorda	.84	.20	.64
5. Cat	1. Chorda	.17	.24	.73
	2. Sym.-on gl. art.	1.24	.24	1.00
	3. Chorda	1.20	.20	1.00

Carlson, Greer, Becht (14). Effect of diminished blood supply to submaxillary gland on solid content of saliva.

These investigators concluded, therefore, that there were secretory nerves to the gland, but that Heidenhain's theory of trophic fibers was superfluous.

Carlson and McLean (15) in working upon cats, dogs, and rabbits, confirmed the results obtained by Carlson, Greer and Becht, and also concluded that, during any single period of activity of the submaxillary gland produced by direct stimulation of the chorda tympani, there is a gradual diminution of the percentage of organic solids in the saliva, independent in some cases of the rate of secretion.

Ex.	Order of samples collected.	Vol. of Saliva.	Solids per 100 c.c. Total.	Inorganic.	Organic.
1.	1.	9.5 c.c.	1.36	.31	1.05
	2.	7.05	1.28	.55	.73
	3.	10.00	1.25	.57	.68
2.	1.	.99	1.63	.25	1.38
	2.	4.85	1.53	.31	1.22
	3.	9.80	1.37	.51	.86
3.	1.	1.17	1.58	.23	1.35
	2.	5.00	1.40	.38	1.02
	3.	9.85	1.33	.48	.85
4.	1.	1.04	1.34	.32	1.02
	2.	4.80	1.23	.52	.71
	3.	9.00	1.05	.36	.69
5.	1.	1.02	1.49	.34	1.15
	2.	4.92	1.21	.55	.66
	3.	9.75	1.45	.60	.80
6.	1.	1.10	2.07	.25	
	2.	4.82	1.85	.30	1.60
	3.	5.10	1.55		1.25
7.	1.	1.05	2.00		
	2.	4.68	2.10	.36	1.74
	3.	5.00	1.84	.59	1.25

Carlson and McLean (15), showing gradual diminution of solids upon continuous stimulation.

Tezner (16) and Chittenden and Richards (17), have worked upon the variations in content of human saliva occuring throughout the day. Their results showed that the saliva is much more concentrated in the morning, and before breakfast, than after the meal. There is also a gradual diminution of the solid content during the afternoon.

The effect of drugs upon the solid content of the saliva has been neglected almost entirely. Chittenden and Richards (17) that reflex stimulation by alcohol, gin, etc., will increase the solids over the content of the normal reflex saliva.

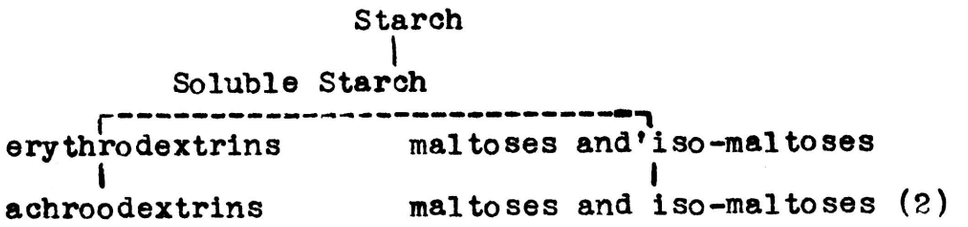
Chittenden, Mendel and Jackson (39), obtained the same results. The following is an extract from their tables:

	2.		4.		5.		7.	
	Water a	Water b	Water a	Brandy b	Water a	Brandy b	Water a	Gin b
Water, per cent.	99.52	99.54	99.50	99.40	99.57	99.19	99.57	99.51
Tot. solids per cent	0.48	0.46	0.50	0.60	0.43	0.81	0.43	0.49
Org. Const. per cent	.35	.33	.35	.45	.31	.58	.31	.35
Salts, per cent	.13	.13	.15	.15	.12	.23	.12	.14

Chittenden, Mendel and Jackson (39) effect of alcoholic drinks upon the solid content of saliva.

Pilocarpine is generally supposed by pharmacologists to increase the total amount of solids, if not the percentage composition of solids of the saliva. (18) I can find no literature upon the effect of atropine upon the content in solids of the saliva.

Variations in Amylolytic Power:- The generally accepted view of hydrolysis of starch by the saliva, is that the starch molecules are converted into maltose by the enzyme ptyalin, the digestion preceding no further, unless long continued, when some inversion occurs. The stages of the digestion are as follows:



Neilson and Scheele (20), however, have come to the conclusion that besides the ptyalin which converts starch into maltose, there is another enzyme "maltase", which inverts the maltose to dextrose, Their results showing that any increase or decrease in ptyalin and maltase is parallel.

Much work has been done on the salivary secretion of mammals, but as the saliva of the dog and cat possesses no amylolytic power few results upon this particular phase of the subject have been obtained. A very interesting variation in the digestive action of saliva is the adaptation of the amylolytic power to the diet. Neilson and Terry (21) when first working upon this problem used the dog experimentally. Contrary to the general belief that dog saliva is not amylolytically active, they concluded that although the saliva of meat-fed dogs showed practically no digestive power, that of continuously bread-fed dogs developed a starch-splitting enzyme.

Gland or saliva.	Wt.	Amt. Water	Amt. 1p.c. starch.	Time in min. of 1st reduction.	Amt. of sugar.
		Dog fed on meat 17 days.			
Sublingual	1.47 g	33 c.c.	60 c.c.	(60 trace of sugar (105 heavy reduction	.049 g
Submaxillary	5.9	65	135	(60 trace (105 heavy reduction	.054
Parotid	1.6	31	62	(50 trace (90 heavy reduction	.071
		Dogs fed on meat 14 days.			
Sublingual	.45	10.	18	60 no sugar 120 " " 180 " " 240 trace sugar	No quantitative determination
Submaxillary	4.55	50.	103	60 no sugar 120 " " 180 " " 240 trace sugar	.029
		Dogs fed on bread 14 days.			
Sublingual	.43	9.5	17.1	60 no sugar 120 sugar at once	
Submaxillary	.41	.46	90.	60 no sugar 120 good reduction)	.041
Parotid	.65	12.4	24.8	60 no sugar 120 trace sugar	

Neilson and Terry (21). Adaptation of dog's saliva to diet.

These results of Neilson and Terry have not been accepted. Garrey (22) in 1907 and Mendel and Underhill (23) have published papers denying that the dog saliva is amylolytically active:

	Exper. 1.	Exper. 2.	Exper. 3.	Exper. 4
	Sal. 20 c.c. Starch paste. Toleune.	Sal. 20 c.c. Starch paste. No Toleune.	Sal. 10 c.c. Toleune.	Sal. 20 c.c. Starch paste. Toleune.
a. Red. next day.	.0117 g cu.	a. faint	a. .001 g cu.	a. faint
b. Iodine test after 2 days.		b. blue		b. blue
c. Iodine test after 9 days.		c. decomposed		c. blue
d. Reduction after 9 days.		d. none		d. positive

Mendel-Underhill (23)- "No evidence of adaptation of amylolytic power." Dog fed on bread 4 to 6 weeks.

Carlson and Ryan (24) have recently reported the presence of diastase in the cat saliva to a small extent, there being a starch-splitting enzyme present, capable of clearing a boiled starch solution.

Saliva	1 c.c. Sal. 5 " Starch paste used.	Time in Hours. 1 1/2	2 1/2	3 1/2	Iodine. 4 1/2
Submaxillary					
1. Chorda stim.	"	clear			red
2. "	" "	"			"
3. "	" "	partly clear.	clear		"
4. "	" "	no	partly clear.	clear	"
5. Pilocarpine injection	"	no clearing	no clearing	"	tinge red
6. Pilocarpine injection	"	"	"	"	
Parotid					
7. Pilocarpine injection	"	"	"	partly clear	blue

Carlson and Ryan (24) Diastase in Cat Saliva.

The work done upon animal saliva has been largely to supplement that upon human saliva. After their experiments upon the adaptation of dog saliva to the diet, Neilson and Lewis (25) worked upon the same problem in regard to the human saliva, concluding that the amylolytic power is adapted to the diet.

Exper.	Control of Diet. maltose av. 3 days.		Percentage change from amt. maltose in control. 1st.	2nd.	3rd.	Diet.	P.C. change from last day prec. ex.		Diet.
W.	120 mg	)Protein	-13	-13	-16	Changed to carbohyd.	7.8	78	Changed to protein
L.	120	)Protein	-7 1/2	-8	-10	Changed to carbohyd.	49	52	Changed to protein
K.	116	)Carbo-	8.6	30	62	Changed to protein.	52	63	Changed to carbohyd.
M.	91	)hydrate	18	20	34	Changed to protein.	25	60	Changed to carbohyd.

Neilson and Lewis (25). Adaptation of human saliva to diet.

The above extract from their tables show conclusively that the saliva of protein-fed individuals reduces the least starch to sugar, and that of carbohydrate-fed subjects the most. The action of mixed diet saliva was taken as a standard of comparison.

Chittenden and Richards (17) obtained some very interesting results from studying the variations in amylolytic power which occur normally throughout the day. They showed that the saliva is much more amylolytically active before the morning meal than afterwards. The curve of digestive power would then gradually increase until the noon meal, and then fall, this decrease being not so decided as that which occured in the morning. Reflex stimulation with alcohol, gin, and whiskey, was found to increase the amylolytic power over that of normal reflex saliva.

Chittenden and Richards also determined the alkalinity of the saliva in these experiments, the results showing that the alkalinity rose and fell with the amylolytic power. At first glance it would seem that the increased digestive action was due to the increased alkalinity of the saliva: Langley and Eves (26) have clearly demonstrated that the amylolytic power of saliva is greatest when the liquid is neutral, so this could not be true.

Further work upon the effect of acids and alkalis upon salivary digestion has been done by Chittenden and Griswold (27). Their results show that acid to .005 per cent increases the diastasic action, while that above .005 per cent decreases and stops the digestion entirely. Alkalis in strength favorable to trypsin digestion do not impede the action of Ptyalin to any extent.

Experiments	1.	2.	3.	4.	5.	6.	7.	8.	9.	Mean ratio.
H_2O	100	100	100	100	100	100	100	100	100	100
.005 HCL	110.0	100.79	104.4	113.32						109.63
.025 "	90.07	54.91	70.94			90.09				76.49
.050 "	9.15	11.95	3.39			.0		43.8		8.21
.005 NaCo					93.87			97.93		95.90
.025 "				89.36	88.27					88.81
.050 "				85.44	81.37				98.15	88.32
.150 "				93.84	64.73					79.28
.300 "								76.90	98.52	87.71
.025 HCl gastric juice						131.19			136.60	133.89
.050 " " "						.00			.00	.00

Chittenden and Griswold (27). Acids and alkalis on diastasic action of saliva.

Chittenden and Ely (28) also determined the effect of peptones upon the digestive action of saliva:

Table of percentage of starch reduced to sugar--

	Without peptones.	With peptones.
1.	41.01 per cent	44.03 per cent
2.	41.69	44.58
3.	41.88	47.58
4.	41.38	44.72
5.	39.13	42.89

	Saliva alone.	Saliva and acid.	Saliva, acid and peptones.
1.	41.01 per cent	3.50 per cent	48.85 per cent
2.	41.69	3.64	48.95
3.	41.88	4.51	48.48

	Saliva alone wt.Cu.in 1/10	Saliva and 50 c.c. NaCo	Saliva, alkali and peptones.
1.	.0905 g	.6 o/o- .0239 g	.0456
2.	.0904	.3 " - .0393	.0685
3.	.1281	.1 " - .0908	.1197

These results show that the addition of peptones increases the diastasic action of saliva. Acid, which alone almost stops the digestive action, augments the normal increase caused by peptones, when mixed with the latter. Although the diastasic action is normally reduced by .6 - .3 - .1 per cent, sodium carbonate solutions, the addition of peptones lessens the decrease one-half.

Neilson and Terry (29) reported that potassium iodide also increases the activity of ptyalin. Their results showed that small quanities, one-fourth to one-half c.c. of a ten per cent solution, when added to a test tube digestion increase the activity of the enzyme the most, although the larger quantities also increase the amylolytic power. Similar results were obtained when the potassium iodide was given by way of the mouth. The normal saliva was collected for three days, and samples after administration of the drug for the same period; the averages of the two series were taken for comparison.

Contents of flask in c.c.		Amt. Maltose produced.
Control-		
Starch paste	75)	
Water	15)	128
Dilute saliva	10)	
Starch paste	75)	
Pot. Iodide 10pc.	15)	140
Dilute saliva	10)	
Starch paste	75)	
Pot. Iodide 10pc.	1/2)	212
Distilled water	14)	
Dilute saliva	10)	

Test tube digestions. Neilson and Terry (29).

No. 1.		Maltose.
Control- average 3 days		17 mg
1st day	150 gr. KI given	40
2nd day	150 " "	50
3rd day	150 " "	65
4th day	150 " "	66
Control- 3 days later		22

Neilson and Terry (29). KI given by way of mouth.

The effect of temperature on enzyme action is well known. Slosse and Linbosch (30), in working upon the effect of temperature upon the activity of ptyalin, found that the digestion increased at a fairly uniform rate from 40 degrees C. up to about 58 degrees C. From there on it decreases rapidly, being practically nothing at 70 degrees. They therefore considered 58 degrees as approximately the optimum temperature for salivary digestion, although this is somewhat higher than is generally accepted: the discrepancies were probably due to variation in the concentration of the digesting solutions.

Another factor which seems to influence enzyme action is the effect of shaking. Shaklee and Meltzer (31) found that shaking may completely destroy the action of pepsin, renin, and trypsin, the destruction taking place more rapidly at higher than lower temperatures.

Harlow (32) obtained similar results when working with saliva and ptyalin. The destruction seems to be upon the enzyme molecules in the same manner in which living cells are acted upon. The long period of shaking necessary to destroy the ferment (eight hours or more) indicates that no attention need be paid it in the ordinary laboratory experiments with ptyalin.

The Action of Pilocarpine and Atropine:- I could find no literature whatever, on the action of pilocarpine or atropine upon the amylolytic power of saliva. Most of the work upon the action of these drugs upon salivary secretion has been largely to determine the variations in volume and the point of action of the drugs. That atropine paralyzes the secretion of saliva, and

that pilocarpine increases and in sufficient doses paralyzes it, has long been known. Langley (33) in working upon the neutral antagonism of the two drugs showed that either drug could prevent the action of the other provided the proper proportions were used. Very small quanities of atropine were found sufficient to counterbalance the action of relatively larger amounts of pilocarpine. The antagonism seems to be physiological, - a question of affinity shown by the tissues for the one drug or the other. Marshall (34) also concluded that the antagonism between the drugs is physiological, the ratio of strengths being about one part of atropine to forty parts of pilocarpine.

The question as to whether or not atropine and pilocarpine act upon the secretory nerve endings, or upon the gland cells themsleves, is at present undecided. The large majority of physiologists have accepted the view that the nerve endings are acted upon and not the cells. This theory is based upon the classic experiment showing that although if sufficient atropine be given to prevent any secretion upon chorda stimulation, excitation of the sympathetic still causes a flow of saliva. For this reason most physiologists have concluded that the gland cells were not paralyzed.

Matthews (35) is one of the recent opponents of this theory. He found that by clamping the artery to the gland, all secretion would stop, and upon readmission of the oxygen supply by unclamping the artery, a rapid flow of saliva occurred.

It will be seen from the following results that the secretion occurring upon readmission of the blood supply is par-

alyzed by atropine, and Mathews concluded, therefore, that the drug must act directly upon the gland cells.

Time. h. m. s.	Stimulation.	Secretion in m.m.
2 - 37 - 10		Clamped artery.
39 - 30		5
39 - 40		2
39 - 41		0
43 -		Unclamped.
43 - 44		2
44 - 45		38
45 - 30	1 c.c. .5 p.c. atropine in femoral vein.	
45 - 46		40
46 - 46		15
46 - 47		6
47 -	Chorda 20 sec.	2
48 -	" " "	0
53 -	Sympathetic 30 sec.	30
53 - 56	" " "	0
56 -	Chorda 20 sec.	0

Mathews (35).

~~It will be seen from the above that the secretion occurring~~

Matthews (36) in another article published some results obtained from studying the effect of atropine and pilocarpine upon embryos. He worked with star fish and sea urchin embryos

and found that their developement was retarded by atropine and hastened by pilocarpine. In applying these results to salivary secretion he concluded that as the animal cells seem to be acted upon directly in the case of embryos, the same is probably true of the salivary cells, any increase or decrease in activity being due to increase or decrease in the oxidative decomposition of the cell protoplasm.

Work upon the metabolism of the submaxillary gland by Barcroft (37) supports that part of the theory concerning the effect of atropine upon oxidation in the gland cells. He showed that three times as much oxygen was taken up and carbon dioxide given off by the active gland (chorda stimulation) as by the resting gland. After paralysis of the chorda secretion by atropine, however, stimulation of the chorda caused no increase in the intake of oxygen, although the output of carbon dioxide was increased as before.

Oxygen intake after chorda paralysis by atropine.

				Total	Mean
Resting gland	.1928	.15	.42	1.04 c.c.	.260 c.c.
Chorda stim.	.1725	.13	.43	.98	.245

Carbon dioxide output after chorda paralysis by atropine.

Resting gland	.22	.13	.41	1.07	.27
Gland stim.	.62	.61	1.28	3.12	.78

Barcroft (37). Metabolism of submaxillary gland.

The supply of oxygen, then, seems to be a most important factor in secretion. The fact that the carbon dioxide output is increased by chorda stimulation after atropine administration probably means that the cells were not entirely paralyzed, and is not a point in favor of Matthew's theory.

SUMMARY OF LITERATURE.

From the preceeding literature, it is seen that the saliva is affected by almost any change in the physical or chemical conditions under which the secretion occurs; the character of the stimulation, food, temperature, chemicals, etc., all cause its properties in volume, solid content and amylolytic power to respond one way or the other. These facts hold good regardless of the theory of "trophic" and "secretory" nerves, which need not be discussed here, although the oxygen supply to the glands seems to be the all important factor in determining the solid content of the saliva. The point of action of the drugs pilocarpine and atropine is also an unsettled question. With this problem the present paper is not primarily concerned. The evidence, however, is in favor of the theory that they act upon the secretory nerve endings, the former drug stimulating and the latter paralyzing them. In looking through the literature, one is struck by the absence of any records of the effect of these drugs, atropine and pilocarpine, upon the physico-chemical properties of the saliva; I shall present in this paper, therefore, some results showing the effect of pilocarpine and atropine upon the volume, amylolytic power, amount and percentage of solid content, organic and inorganic, of the human saliva, without taking into special consideration the specific point of action of the drugs.

EXPERIMENTAL.

Collection of Saliva:- The reflex secretion of saliva was excited by chewing ordinary paraffin. The collection was always made in the morning before breakfast, so that the glands would be in an approximately constant condition of rest before the period of secretion. Dr. R. B. Gibson alternated with me in collecting the saliva for the experiments. The results show the variations to be practically the same for the two individuals.

I had intended to collect normal samples for several days, and then samples for several days showing the drug effects, and average the two series for comparison. Tables 1 and 7 are of some results obtained with this method. The normal samples, however, show such great variations from day to day that I decided that I could arrive at no definite conclusions by this method. In the remaining experiments the saliva was collected in separate samples for consecutive fifteen minute periods, during the entire time of the secretion, which was usually of about an hour and a half to two hours duration. Six or eight samples collected in this way served as a control, and also furnished interesting results concerning the normal variations in saliva during a continuous period of secretion.

For the drug experiments , I would collect normal saliva for the first fifteen minute period as the control, take the atropine or pilocarpine, and proceed with the collection of samples which would show the variations caused by the drug.

In this way the time of maximal and minimal effect of the drug could be determined, and by collecting the first sample as a control, any error due to change of the normal standard for amylolytic power and solid content during the last twenty-four hours was eliminated when comparing the normal and drug variations.

Determination of the Amylolytic Power:- In determining the amylolytic power of the various samples of saliva, I proceeded as follows: 5 c.c. of filtered saliva were added to 150 c.c. of two per cent starch paste prepared from pure arrow root starch. The digestion which continued at room temperature for twenty minutes. It was then stopped by the addition of 50 c.c. of twenty per cent sodium carbonate solution. This method of stopping the digestion with strong alkali solution is an improvement, I believe, over the usual method of boiling the mixture; it is much more convenient, and the exact time of digestion is much more accurately controlled.

The amount of maltose produced was then determined by Benedict's (38) method. A mixture of 10 c.c. of each of the solutions A, B, C, was used for each titration.

Solution A.	Crystallized Copper Sulphate	69.30 g
	Distilled Water	1000 c.c.
Solution B.	Rochelle Salts	346 g
	Sodium Carbonate	200 g
	Distilled Water	1000 c.c.
Solution C.	Potassium Sulpho Cyanide	200 g
	Distilled Water	1000 c.c.

2.5 grams to 5 grams of sodium carbonate were added to the mixture of the solutions in order to increase the alkalinity and thus obtain a more definite end point. This mixture was kept boiling vigorously in a small beaker , while the digestive starch paste plus sodium carbonate solution was run in slowly until the blue color of the mixture had entirely disappeared; this is the end point of the titration. As Benedict's formula was for dextrose, I ran some one per cent maltose solution control titrations, and found that the 10 c.c. of copper sulphate solution was equivalent to approximately .115 grams of maltose, theequation for determining the amount of maltose produced being:

$$y : .115\ g = 100 : x$$

Titration

Determination of Total Solids and Ash:- For the determination of the content in total solids, the standard method of drying in low porcelain crucibles on the water bath, then in the air bath at 105 degrees C., was employed. The residue was weighed for the total solids, ashed, and weighed again to determine the content of inorganic solids. The difference between the two results thus obtained was taken as the content of organic constituents.

A definite quantity, 5c.c. of filtered saliva, was used in all of these determinations for content in solids.

CONTROL OBSERVATIONS.

The value of my results showing the effects of pilocarpine and atropine, necessarily depended entirely upon the control observations which were used for comparison. Accordingly I performed a number of experiments to ascertain any variations which might occur in normal saliva throughout the six or eight consecutive fifteen minute periods of secretion.

The variations shown in Table 1, in saliva collected on different days, demonstrated the impossibility of using the normal results of one day as a control for accurate drug effects on the next. These variations, though not great, were enough to eliminate any definite conclusions as to the constancy of normal saliva, or of the variations caused by the drugs. At the same time they serve to illustrate the changes in the normal composition of saliva from day to day. For samples within a period of three days, the volume had changed 14 c.c., the amylolytic power 130 mg. of maltose produced, and the content in total solids .08 per cent.

The results obtained from the saliva collected in consecutive fifteen minute periods, however, showed very little variation throughout the period of secretion, and therefore served as good controls for the drug experiments.

My results are tabulated, but the charts which I have made for each table, show at a glance any variations which may occur. Chart 2A shows the <u>volume</u> of saliva secreted per fifteen minute period, to be approximately constant for the six consecu-

tive periods. Although there are both increases and decreases in some of the experiments, I have found that these changes coincide with any variation in the strength whith which I chewed the paraffin, and that even at the last of my longest experiments, I could always increase the volume by additional stimulation of the glands in this way.

Amylolytic Power:- Chart 3A shows that the amylolytic power also remains approximately constant throughout the periods of secretion. From the line of average variation it appears that there may be a very slight falling off during one or two of the fifteen minute periods, but that the amount of maltose produced is usually just as great for the last period as for the first.

Content in Solids:- In making up my tables I have computed not only the variations in the percentage composition of the solid content, but also the actual amount of solids secreted during each of the entire fifteen minute periods.

Both the amount and percentage of total solids seem to remain practically the same throughout the experiments, with the exception of Experiments 1 - 3, where error in technique probably cause the variations. An average of the variations of Experiment 3 - 9 shows that any change which occurs, is a very slight diminishing of both amount and percentage composition usually in the second period of secretion.

Practically the same can be said of the amount and percentage of organic solids, - Chart 5A.

Chart 6A shows the amount and percentage of inorganic solids to be constant, so the slight falling off of total solids is due to the change occurring in the organic solid content.

Summary of Control Observations:- From the above it seems, therefore, that the results obtained from a series of samples collected in consecutive fifteen minute periods, would serve as good controls for comparison with the drug variations. What changes did occur, were entirely in accordance with the literature reviewed,- that the volume changes with the strength of stimulus, and that there is a decrease in the organic solids during a continuous period of secretion, (15). The diminution of organic solids in my experiments, however, was not a gradual decrease such as Carlson and McLean (15) obtained with a cat, but occurred in most cases about the second period of secretion, the amount and percentage composition usually being back to normal during the fifth and sixth periods.

At any rate I do not believe that there was sufficient change in any of the physico-chemical properties of the normal saliva to need special consideration when they were compared with any decided drug effects.

Table 1.

Collector	E.						G.		
Date of Exper.	1-7-09	1-10	1-11	1-12	1-13	1-15	1-14	1-17	1-20
Vol. c.c.	16	21	20	21	30	21	35	30	27
Amylolytic power g. maltose.	.718	.676	.718	.575	.580	.851	.234	.469	.605
Total solids percentage.	.46	.54	.52	.48	.54	.46	.56	.54	.58
Percentage org. solids.	.34	.48	.40	.36	.38	.38	.50	.40	.48
Percentage inorg. solids.	.12	.06	.12	.12	.16	.08	.06	.14	.10

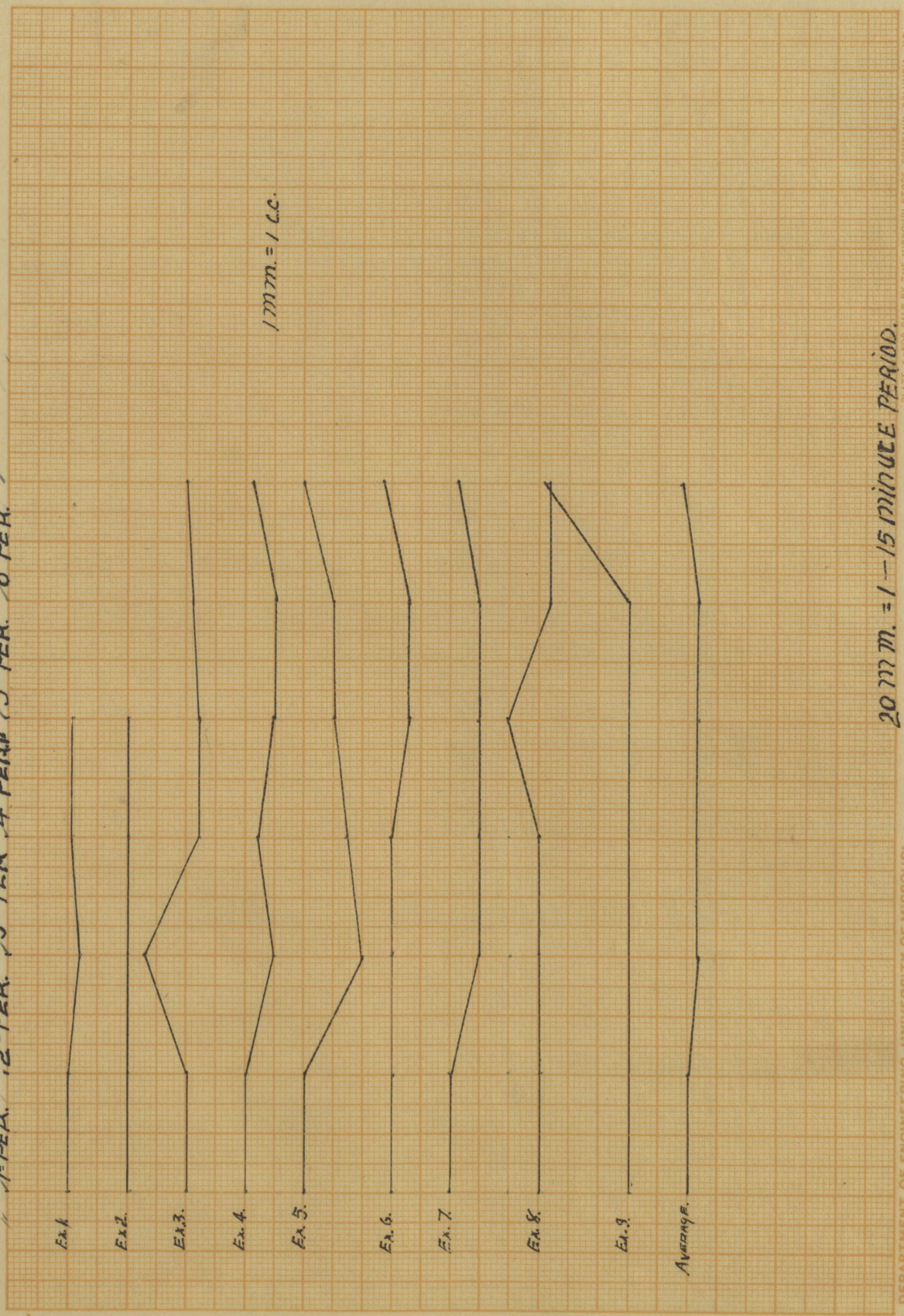
Normal Variations in Saliva:- Collections made during a period of 7 days.

Table 2.

Ex.	Col.	Samples collected in consecutive 15 min. periods. Volumes in c.c.							
		Per. 1	Per. 2	Per. 3	Per. 4	Per. 5	Per. 6	Per. 7	Per. 8
1.	E. Vol.	20	18	20	20				
2.	E. Vol.	18	18	18	18				
3.	G. Vol.	40	48	38	38	39	40		
4.	G. Vol.	45	40	43	40	40	43	37	
5.	E. Vol.	40	30	33	35	35	40		
6.	E. Vol.	33	33	33	30	30	35		
7.	E. Vol.	35	30	30	30	30	33		
8.	E. Vol.	20	20	20	25	18	18		
9.	E. Vol.	25	25	25	25	25	35		

Normal Variations in Volume.

Chart 2A.



Normal Variations in Volume.

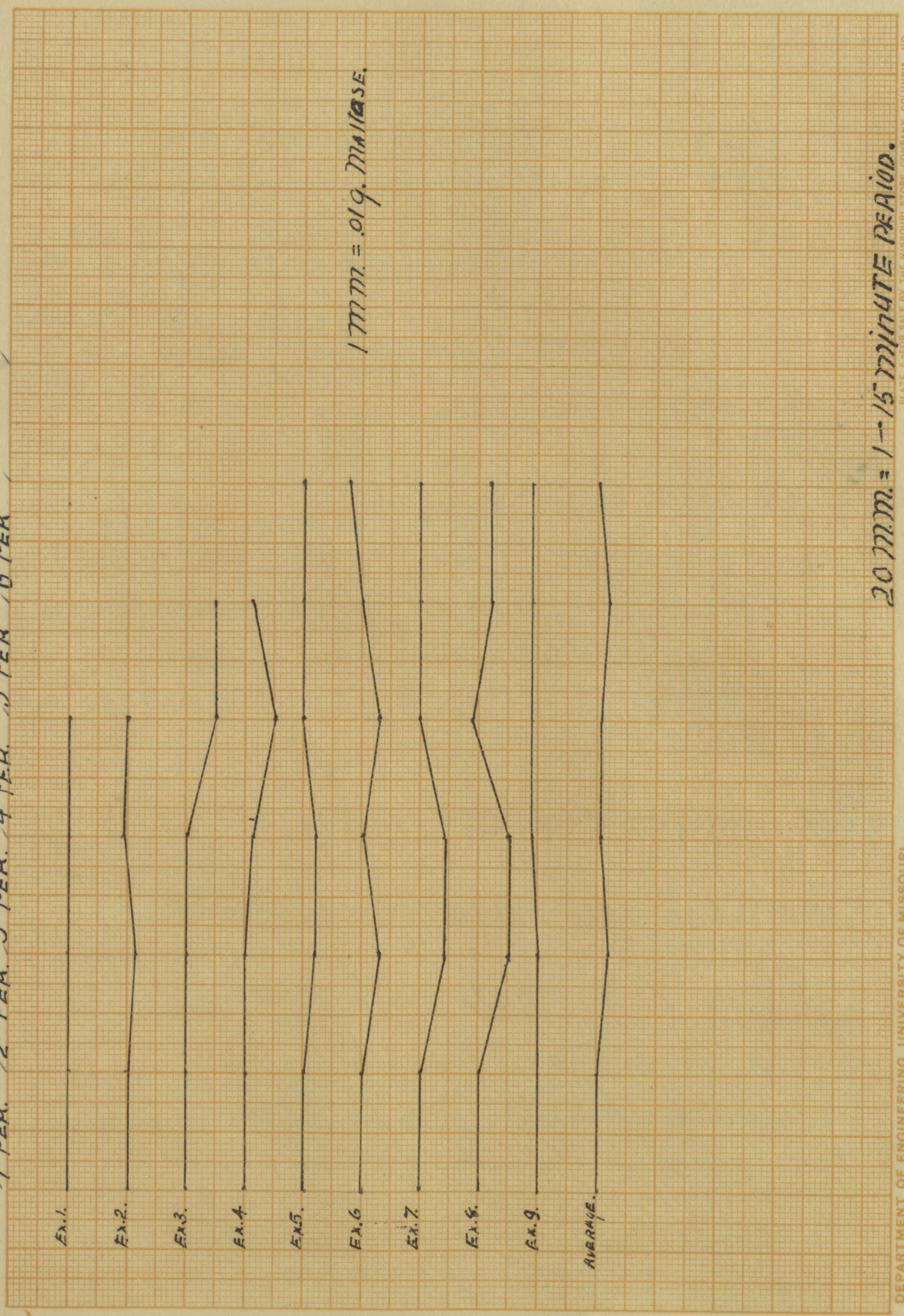
Table 3.

Grams of maltose produced by samples collected in consecutive 15 minute periods.

Ex.	Col.	Per. 1	Per. 2	Per. 3	Per. 4	Per. 5	Per. 6
1.	E.	.821g	.821	.821	.821		
2.	E.	.696	.685	.696	.685		
3.	G.	.469	.460	.460	.460	.425	.425
4.	G.	.766	.756	.746	.718	.718	.741
5.	E.	.522	.506	.500	.522	.522	.522
6.	E.	.522	.479	.471	.522	.479	.479
7.	E.	.500	.479	.500	.479	.500	.522
8.	E.	.718	.676	.676	.718	.718	.718
9.	E.	.756	.766	.766	.766	.766	.766

Normal Variations in Amylolytic Power.

Chart 3A.



Normal Variations in Amylolytic Power.

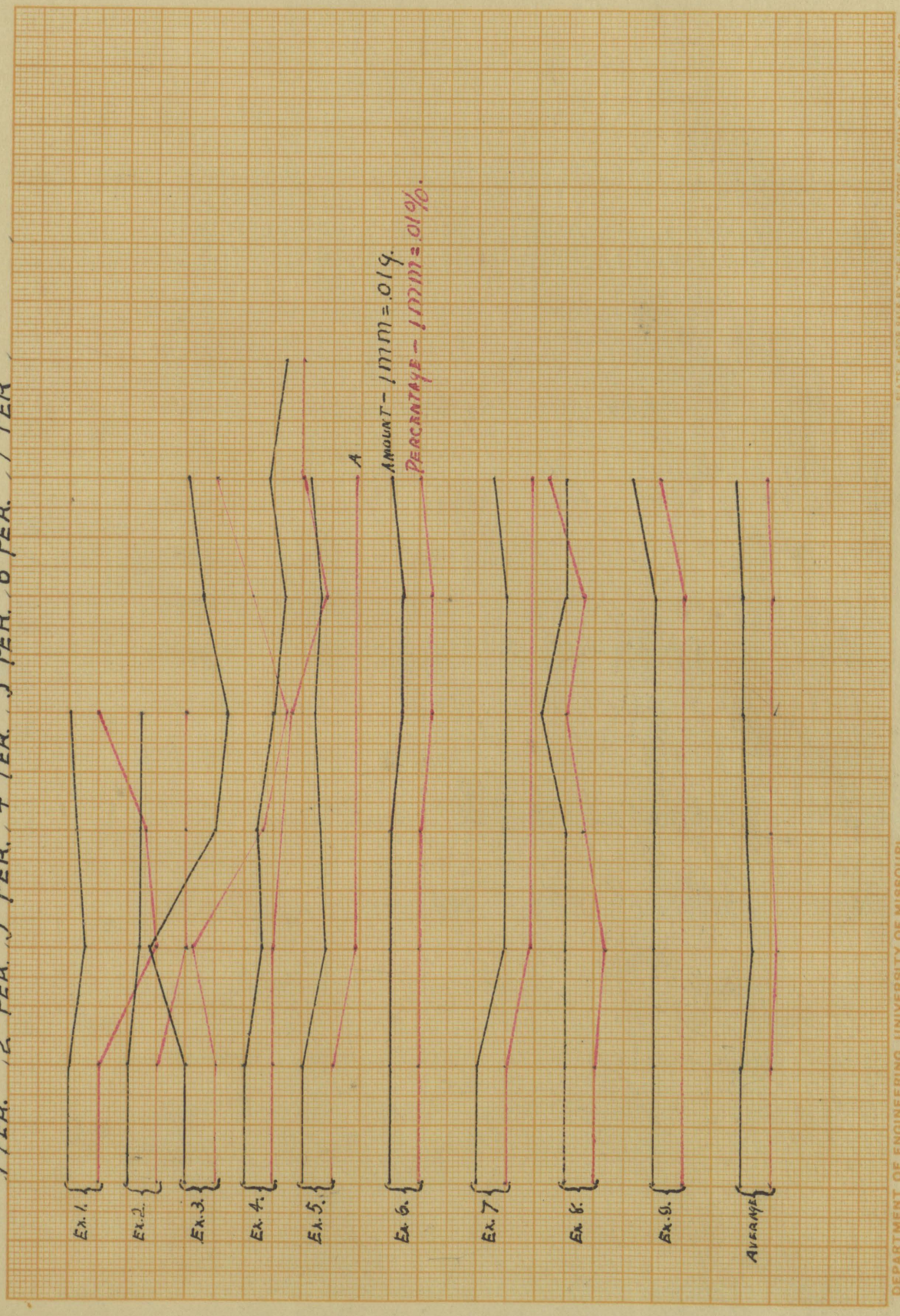
Table 4.

Total Samples collected in consecutive 15 min. periods.

Ex.	Col.	Solids	Per. 1	Per. 2	Per. 3	Per. 4	Per. 5	Per. 6	Per. 7
1.	E.	Amt. secreted.	.104 g	.0756	.088	.104			
		Percentage.	.52	.42	.44	.52			
2.	E.	Amount	.0952	.0756	.072	.075			
		Percentage.	.56	.42	.40	.42			
3.	G.	Amount	.240	.307	.197	.182	.210	.244	
		Pctg.	.60	.64	.52	.48	.54	.60	
4.	G.	Amount	.297	.264	.275	.248	.224	.258	.222
		Pctg.	.66	.66	.64	.62	.56	.60	.60
5.	E.	Amount	.176	.120	.132	.140	.140	.160	
		Pctg.	.44	.40	.40	.40	.40	.40	
6.	E.	Amount	.132	.132	.132	.114	.114	.140	
		Pctg.	.40	.40	.40	.38	.38	.40	
7.	E.	Amount	.152	.102	.102	.102	.102	.112	
		Pctg.	.38	.34	.34	.34	.34	.34	
8.	E.	Amount	.076	.072	.080	.120	.072	.082	
		Pctg.	.38	.36	.40	.44	.40	.46	
9.	E.	Amount	.100	.100	.100	.100	.100	.154	
		Pctg.	.40	.40	.40	.40	.40	.44	

Normal Variations in Total Solid Content.

Chart 4A.



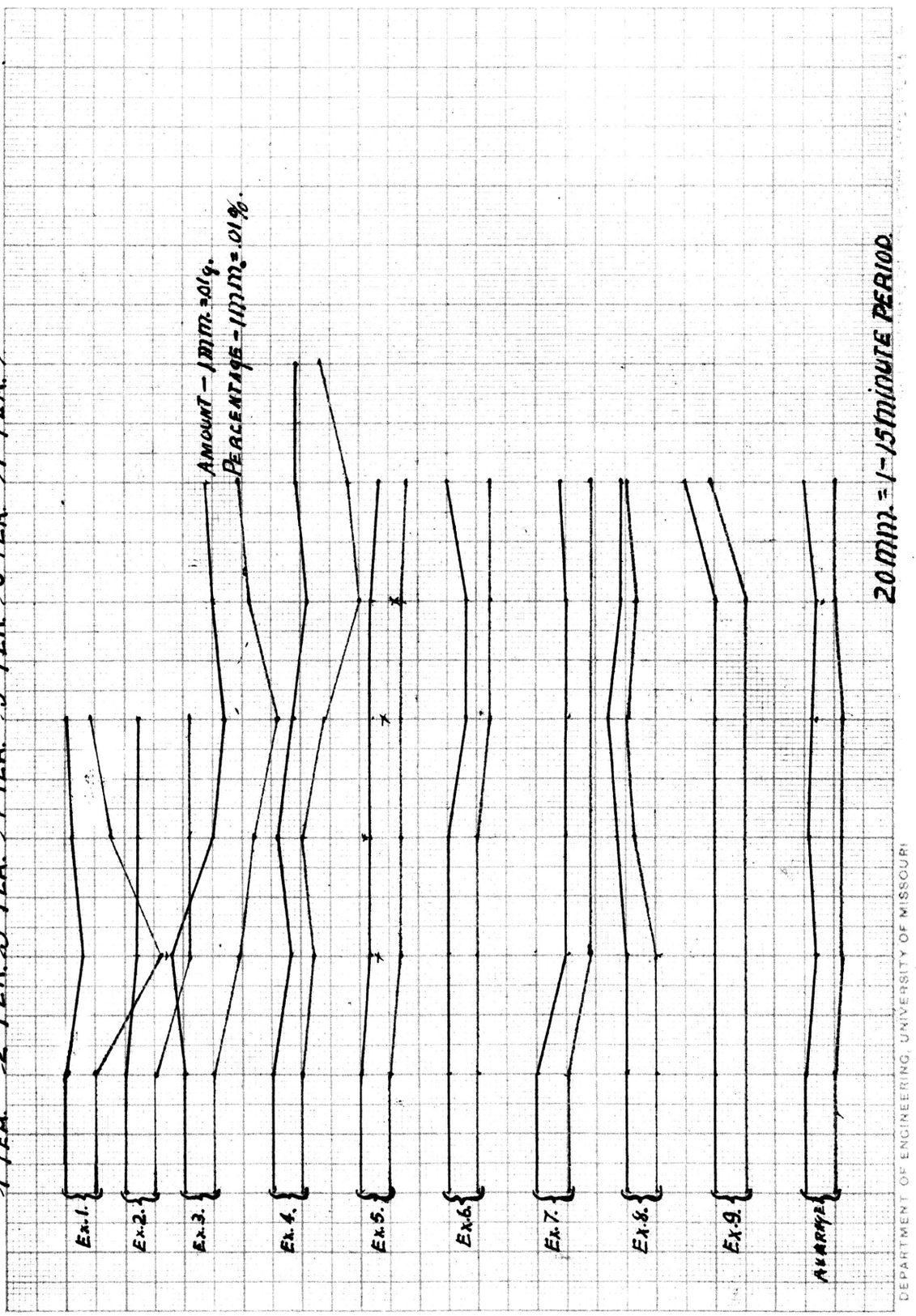
Normal Variations in Total Solid Content.

Table 5.

Ex.	Col.	Organic Solids.	Samples collected in consecutive 15 min. periods. Per. 1	Per. 2	Per. 3	Per. 4	Per. 5	Per. 6	Per. 7
1.	E.	Amount secreted	.080 g	.0504	.072	.084			
		Pctg. vol. secreted.	.40	.28	.36	.42			
2.	E.	Amount	.071	.054	.054	.054			
		Pctg.	.42	.30	.30	.30			
3.	G.	Amount	.208	.230	.152	.136	.156	.172	
		Pctg.	.52	.48	.40	.36	.40	.43	
4.	G.	Amount	.207	.176	.197	.168	.144	.163	.162
		Pctg.	.46	.44	.46	.42	.36	.38	.44
5.	E.	Amount	.128	.084	.092	.098	.098	.104	
		Pctg.	.32	.28	.28	.28	.28	.26	
6.	E.	Amount	.092	.092	.092	.066	.066	.091	
		Pctg.	.28	.28	.28	.26	.26	.26	
7.	E.	Amount	.120	.078	.078	.078	.078	.085	
		Pctg.	.30	.26	.26	.26	.26	.26	
8.	E.	Amount	.048	.048	.056	.085	.059	.054	
		Pctg.	.24	.24	.28	.30	.28	.32	
9.	E.	Amount	.70	.70	.70	.70	.70	.119	
		Pctg.	.28	.28	.28	.28	.28	.34	

Normal Variations in Organic Solid Content.

Chart 5A.



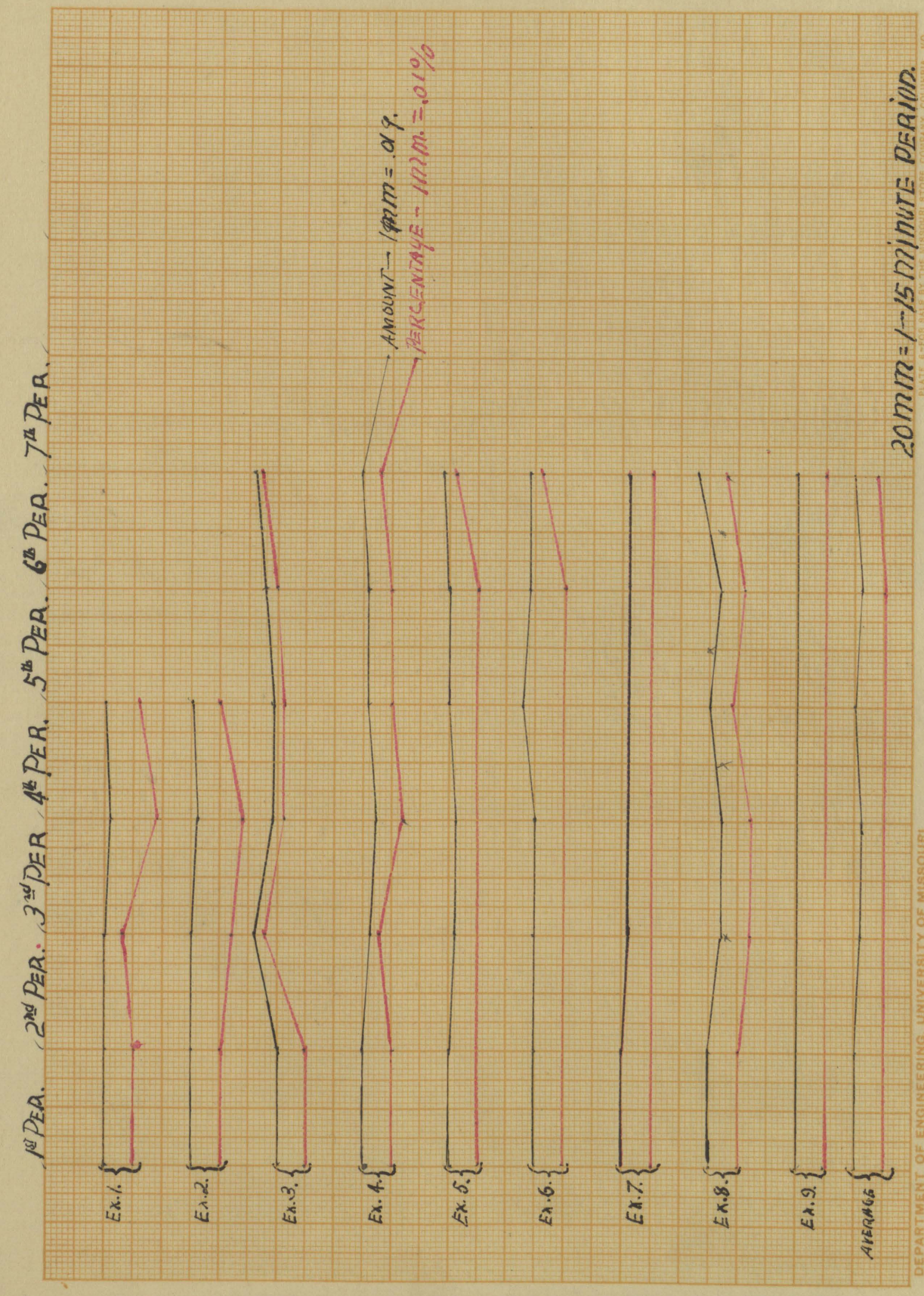
Normal Variations in Organic Solid Content.

Table 6.

Ex.	Col.	Inorg. Sol.	Samples collected in consecutive 15 min. Periods.						
			Per. 1	Per. 2	Per. 3	Per. 4	Per. 5	Per. 6	Per. 7
1.	E.	Amt. Secreted	.024 g	.025	.016	.020			
		Percentage	.12	.14	.08	.10			
2.	E.	Amount	.0238	.0216	.018	.0216			
		Percentage	.14	.12	.10	.12			
3.	G.	Amount	.032	.076	.045	.045	.054	.072	
		Percentage	.08	.16	.12	.12	.14	.17	
4.	G.	Amount	.09	.08	.07	.08	.08	.09	.05
		Percentage	.20	.22	.18	.20	.20	.22	.16
5.	E.	Amount	.048	.036	.039	.042	.042	.056	
		Percentage	.12	.12	.12	.12	.12	.14	
6.	E.	Amount	.039	.039	.039	.048	.048	.049	
		Percentage	.12	.12	.12	.12	.12	.14	
7.	E.	Amount	.032	.024	.024	.024	.024	.026	
		Percentage	.08	.08	.08	.08	.08	.08	
8.	E.	Amount	.028	.024	.024	.035	.021	.028	
		Percentage	.14	.12	.12	.14	.12	.16	
9.	E.	Amount	.030	.03	.03	.03	.03	.035	
		Percentage	.12	.12	;12	.12	.12	.10	

Normal Variations in Inorganic Solid Content.

Chart 6A.



Normal Variations in Inorganic Solid Content.

VARIATIONS AFTER ADMINISTRATION OF PILOCARPINE.

With it established that the properties of saliva remain approximately the same throughout the six periods of secretion, I proceeded with the experiments showing the effect of pilocarpine.

Normal saliva was collected for the first fifteen minute period as the control, the drug was then swalloed in a gelatine capsule, and the collection continued without further intermission. The succeeding samples show not only the drug effect upon the properties of the saliva, but also the point of maximal and minimal change.

Volume:- The well known effect of pilocarpine upon the volume secreted is shown by Chart 8A, and need not be discussed, except to mention that the maximal increase appears to occur about the third period in the case of the smaller doses; the volume remains high after the larger doses until the experiment was concluded.

Amylolytic Power:- The amylolytic power of the saliva is very materially diminished by pilocarpine, a decrease occurring in every experiment performed, - Chart 9A. There seems to be no definite relation between the quantity of the drug taken and the decrease in amount of maltose produced. For instance, in Experiment 4 with a dose of .005 grams of pilocarpine there was a decrease of 328 mg. of maltose, - in Experiment 6 with .01 grams of pilocarpine there was a decrease of 366 mg. of maltose, - while in Experiment 8 after a dose of .013 grams of the drug, there was

only a decrease of 129 mg. of maltose produced. The amylolytic power appears to be lowest about the second period after administration of the drug.

Content in Solids:- The results in Table 10 and Chart 10A show that pilocarpine largely increases the actual amount of total solids secreted, but that the percentage of total solids remains more nearly normal. From the line of average percentage variations, it seems that if there is any change in the percentage composition of total solids, it is an increase, and not a decrease as stated by Sollman (18).

Charts 11A and 12A show that these changes, i.e., an increase in amount and percentage of total solids, - are due to increase in amount and percentage of both the organic and inorganic constituents. The greatest variation, however, appears to occur in the amount of the organic solids secreted.

The maximal increase in solid content seems to occur in the second period after the administration of the pilocarpine.

Summary of Effect of Pilocarpine:- Whether or not the increase in volume after pilocarpine, is caused by stimulation of the secretory nerve endings, or by direct action upon the gland cells, need not be discussed in this paper. Suffice it to say that my results showed the same increase in volume obtained by former investigators.

The amylolytic power of the saliva was diminished by the small doses as well as by the large ones. In the majority of the experiments it remained low longer after the larger doses

than after the smaller ones.

There does not seem to be any relation between the volume secreted and the amylolytic power. For instance, in Experiment 5, the normal volume and amylolytic power were 19 c.c. and 766 mg. of maltose, respectively, while in the fourth period of this experiment the volume secreted was 50 c.c., and the amylolytic power had come back to normal,- 766 mg. of maltose were produced.

From the increase in solids that my results show, I would infer that the "trophic" as well as the "secretory" fibers, or cell elements, are stimulated to increased activity by pilocarpine.

Another point brought out in Table 7 appears to illustrate the acquired tolerance for pilocarpine mentioned by some of the old investigators, (34). Here the results show that the same dose of the drug when given several times, gradually decreases in its effect upon the properties of the saliva. I made no special study of acquired tolerance for the drug in this work, but simply mention it as my explanation for the decreased action of the same quantity of pilocarpine, as shown by the results in Table 7.

Table 7.

Date and Dose	Control 1-14-09	Pilo..003g 1-15-09	.003 Pilo. 1-16-09	.003 Pilo. 1-17-09	.004 Pilo. 1-19-09
Volume	21 c.c.	45 c.c.	30 c.c.	28 c.c.	45 c.c.
Amy. Power g. Maltose.	.851	.323	.403	.676	.493
Pctg. Tot. Solids	.46	.52	.40	.46	.46
Pctg. Org. Solids	.38	.36	.34	.32	.28
Pctg. Inorg. Solids	.08	.16	.06	.14	.18

Variations in Saliva after Administration of Pilocarpine.

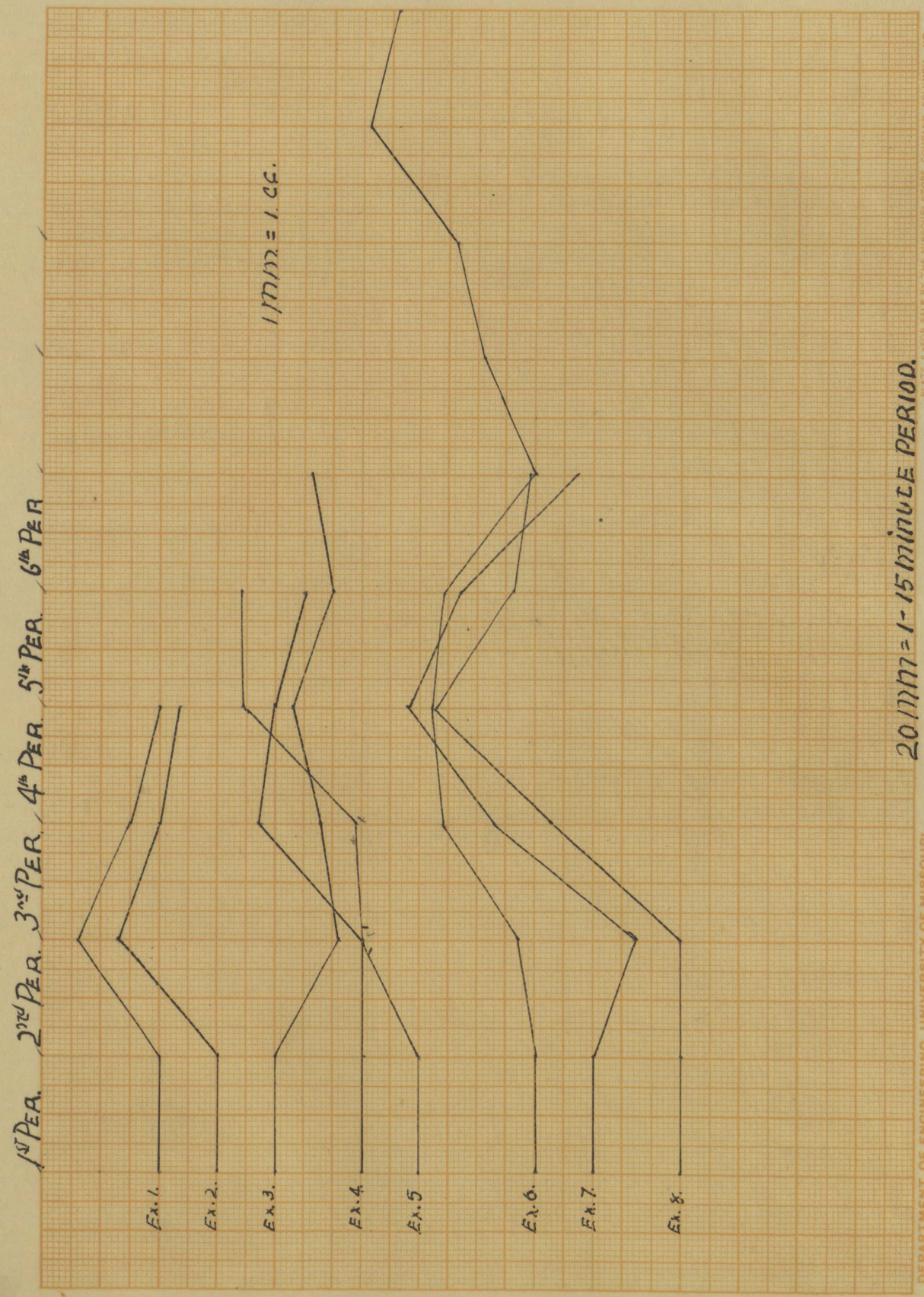
(Collections made on consecutive days.)

Table 8.

Exper. and Collector	Control 15 min. Period.	Volume in c.c. after drug samples collected in consecutive 15 min. periods. Per. 2	Per. 3	Per. 4	Per. 5	Per. 6	Per. 7	Per. 8	Per. 9
1. E.	.004	25	39	30	25				
2. E.	.004	18	36	28	25				
3. G.	58 cc .005	47	50	55	48	52			
4. E.	25 .005	25	43	41	35				
5. E.	19 .010	28	30	50	50				
6. G.	37 .010	40	54	55	53	36	45	50	40
7. EF	37 .010	30	55	70	60	52	45		
8. E.	33 .013	33	56	75	61	59			

Variations in Volume after Administration of Pilocarpine.

Chart 8A.



Variations in Volume after Administration of Pilocarpine.

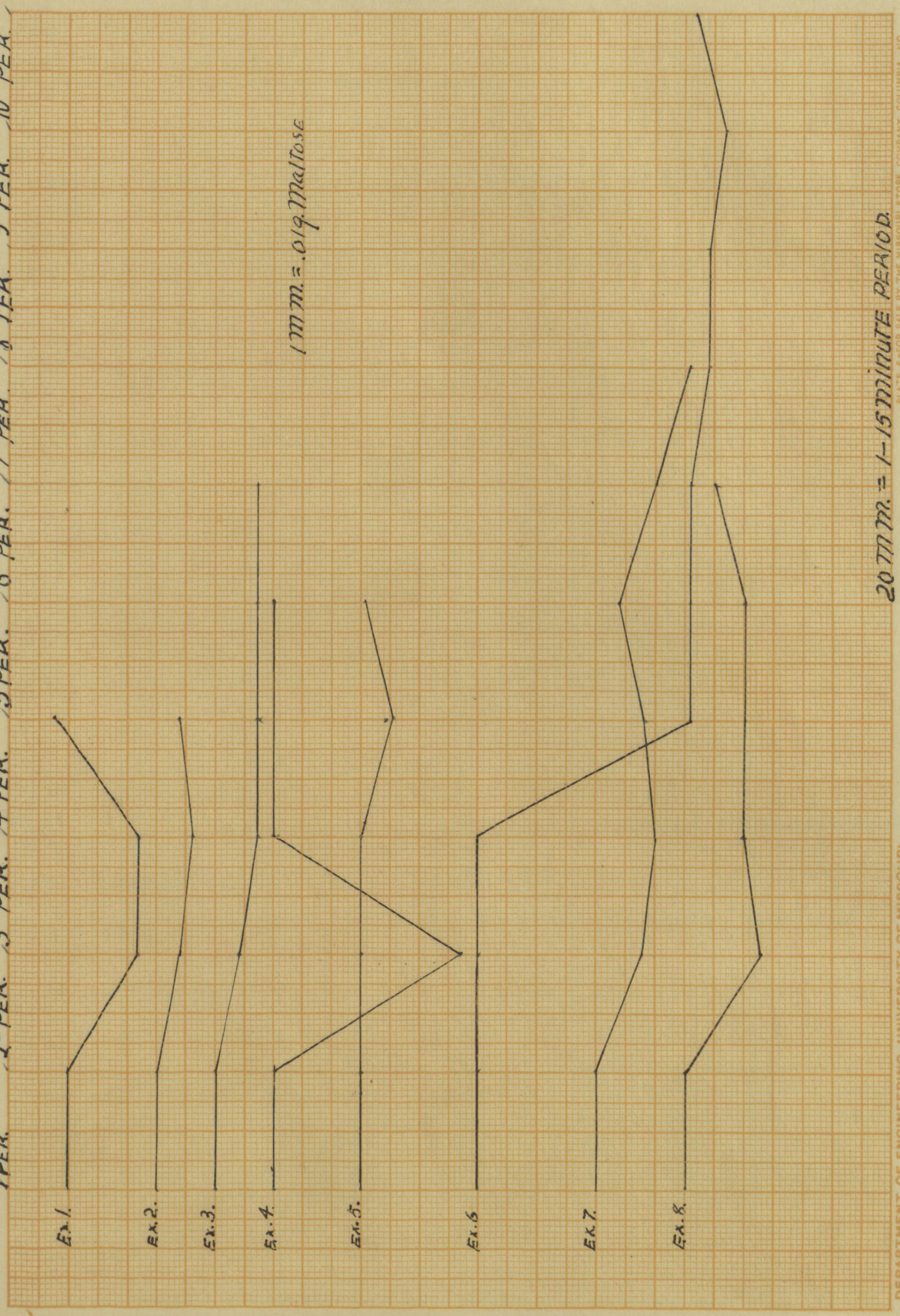
Table 9.

Exper. and Coll.	Control 15 min. Period	Pilocarpine.	Grams Maltose produced after drug samples collected in consecutive 15 min. periods. Per. 2	Per. 3	Per. 4	Per. 5	Per. 6	Per. 7	Per. 8	Per. 9	Per. 10
1. E.		.004g	.547	.425	.433	.575					
2. E.		.004	.267	.230	.182	.209					
3. G.	.389g	.005	.343	.323	.323	.319	.323				
4. E.	.821	.005	.493	.821	.821	.821					
5. E.	.766	.010	.756	.766	.718	.766					
6. G.	.676	.010	.676	.676	.310	.310	.319	.287	.281	.255	.287
7. E.	.442	.010	.370	.348	.359	.383	.323	.255			
8. E.	.676	.013	.547	.575	.575	.575	.638				

Variations in Amylolytic Power after Administration of Pilocarpine.

N.B. This table shows the relative digestive activity of the saliva before and after pilocarpine,- 5c.c. of the saliva were used in each digestion, irrespective of the total volumes secreted for the various 15 minute periods.

Chart 9A.



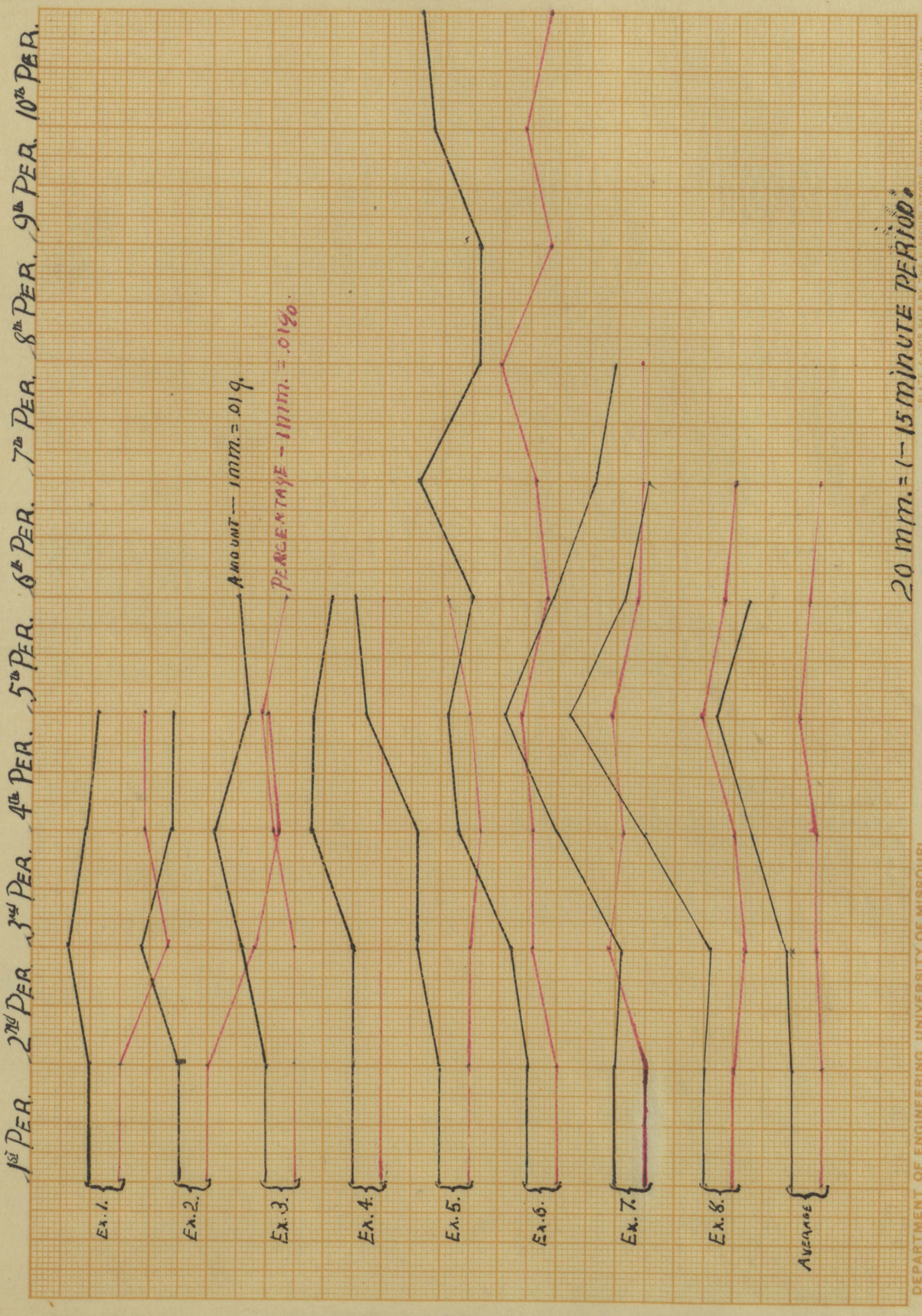
Variations in Amylolytic Poer after Administration of Pilocarpine.

Table 10.

Exper. and Coll.	Total solids	Samples collected in consecutive 15 min. periods, drug taken between periods 1 and 2.								
	Control Per. 1	Pilo. taken	Per. 2	Per. 3	Per. 4	Per. 5	Per. 6	Per, 7	Per. 8	Per. 9
1. Amt. Sec.		.004g	.125	.163	.138	.115				
E. Pctg.			.50	.42	.46	.46				
2. Amt.		.004	.090	.151	.106	.100				
E. Pctg.			.50	.42	.38	.40				
3. Amt.	.348	.005	.282	.320	.374	.297	.332			
G. Pctg.	.60		.60	.64	.68	.62	.64			
4. Amt.	.110	.005	.110	.189	.180	.154				
E. Pctg.	.44		.44	.44	.44	.44				
5. Amt.	.076	.010	.112	.114	.200	.220				
E. Pctg.	.40		.40	.38	.40	.44				
6. Amt.	.222	.010	.256	.345	.363	.328	.416	.315	.310	.396
G. Pctg.	.60		.64	.64	.66	.62	.64	.70	.62	.66
7. Amt.	.1628	.010	.150	.264	.350	.276	.208	.180		
E. Pctg.	.44		.50	.48	.50	.46	.40	.40		
8. Amt.	.145	.013	138	.246	.375	.280	.259			
E. Pctg.	.44		.42	.44	.50	.46	.44			

Variations in Total Solid Content after Administration of Pilocarpine.

Chart 10A.



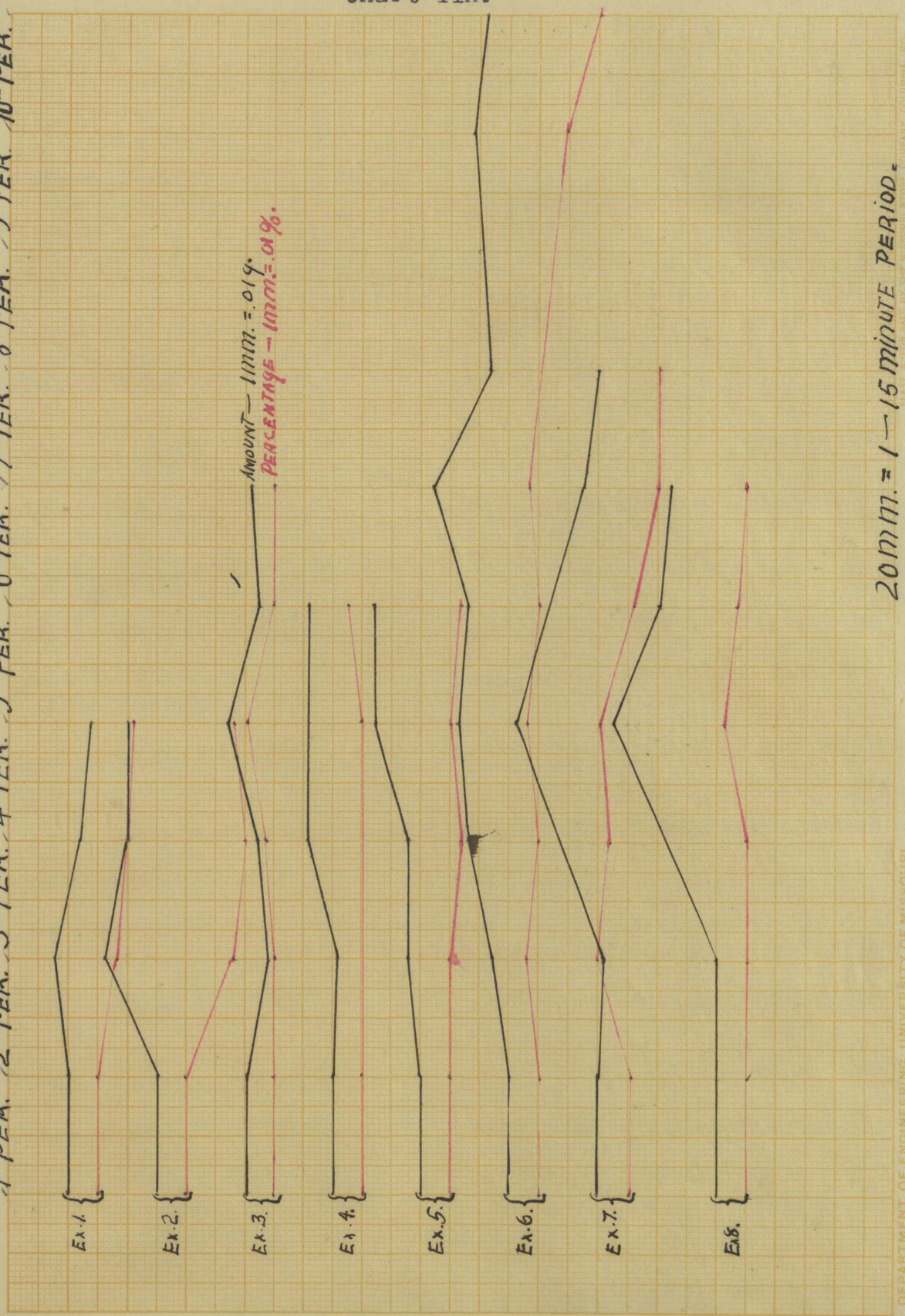
Variations in Total Solid Content after Administration of Pilocarpine.

Table 11.

Exper. and Coll.	Org. Solids	Control Per. 1	Pilocarpine.	Samples collected in consecutive 15 min. periods, drug taken between periods 1 and 2. Per. 2	Per. 3	Per. 4	Per. 5	Per. 6	Per. 7	Per. 8	Per. 9
1.	Amt. Sec.		.004g	.100	.124	.096	.075				
E.	Pctg.			.40	.32	.32	.30				
2.	Amt.		.004	.079	.115	.084	.080				
E.	Pctg.			.44	.32	.30	.32				
3.	Amt.	.243	.005	.197	.220	.275	.211	.228			
G.	Pctg.	.42		.42	.44	.50	.44	.44			
4.	Amt.	.090	.005	.090	.154	.147	.133				
E.	Pctg.	.36		.36	.36	.36	.38				
5.	Amt.	.053	.010	.078	.078	.140	.130				
E.	Pctg.	.28		.28	.26	.28	.26				
6.	Amt.	.162	.010	.184	.237	.253	.233	.299	.189	.200	.228
G.	Pctg.	.44		.46	.44	.46	.44	.46	.42	.40	.38
7.	Amt.	.111	.010	.108	.187	.252	.192	.135	.117		
E.	Pctg.	.30		.36	.34	.36	.32	.26	.26		
8.	Amt.	.105	.013	.105	.179	.285	.207	.188			
E.	Pctg.	.32		.32	.32	.36	.34	.32			

Variations in Organic Solid Content after Administration of Pilocarpine.

Chart 11A.



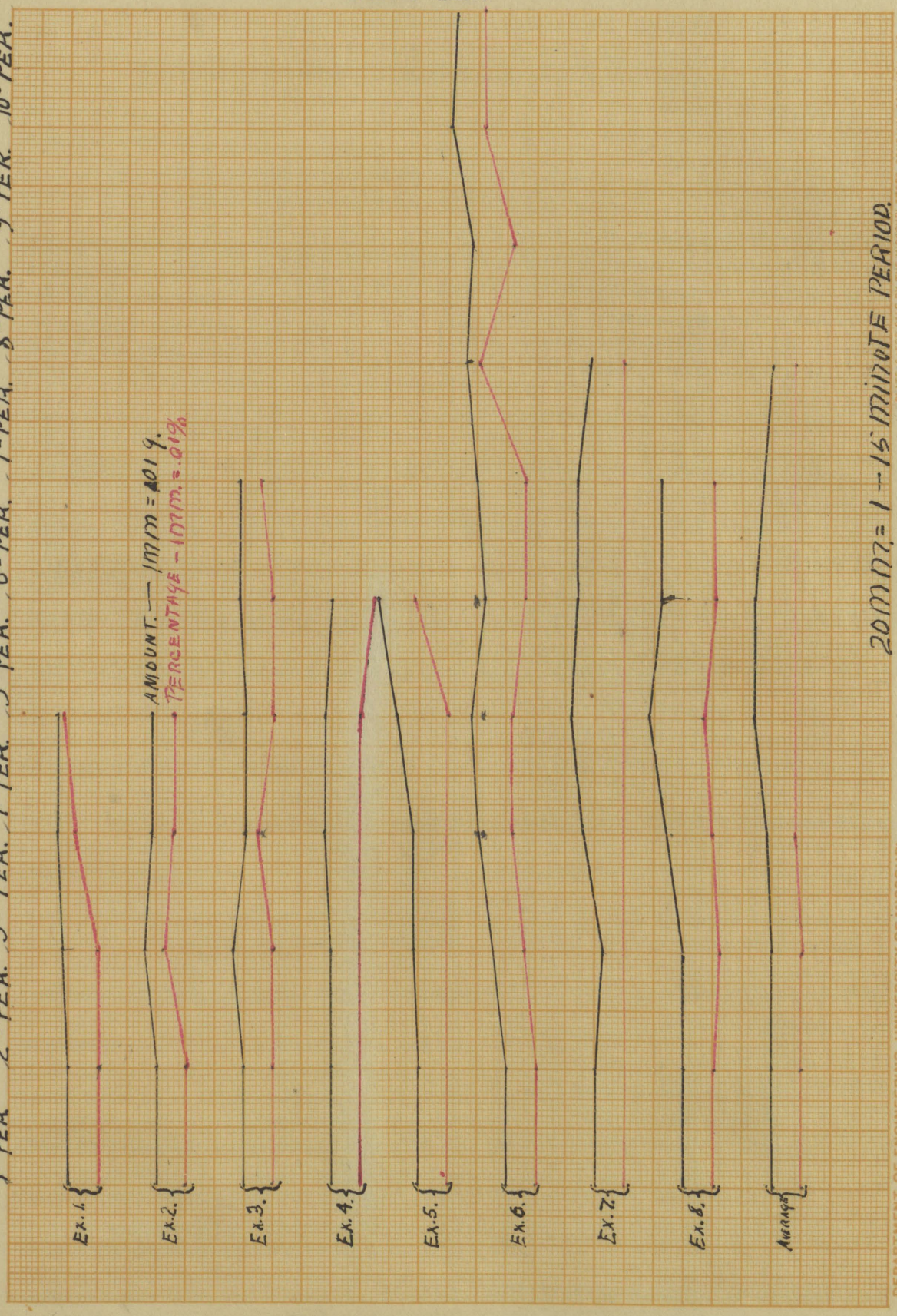
Variations in Organic Solid Content after Administration of Pilocarpine.

Table 12.

Exper. and Coll.	Inorg. Solids.	Samples collected in consecutive 15 min. periods, drug taken between periods 1 and 2.								
		Control Per. 1	Pilocarpine.	Per. 2	Per. 3	Per. 4	Per. 5	Per. 6	Per. 7	Per. 8
1.	Amt. Sec.		.004g	.025	.039	.042	.040			
E.	Pctg.			.10	.10	.14	.16			
2.	Amount		.004	.010	.036	.022	.020			
E.	Pctg.			.06	.10	.08	.08			
3.	Amount	.104	.005	.084	.100	.099	.086	.104		
G.	Pctg.	.18		.18	.20	.18	.18	.20		
4.	Amount	.020	.005	.020	.034	.032	.021			
E.	Pctg.	.08		.08	.08	.08	.06			
5.	Amount	.022	.010	.033	.036	.060	.09			
E.	Pctg.	.12		.12	.12	.12	.18			
6.	Amount	.059	.010	.072	.108	.110	.095	.117	.126	.110
G.	Pctg.	.16		.18	.20	.20	.18	.18	.28	.22
7.	Amount	.051	.010	.042	.077	.098	.084	.072	.063	
E.	Pctg.	.14		.14	.14	.14	.14	.14	.14	
8.	Amount	.039	.013	.033	.067	.090	.073	.070		
E.	Pctg.	.12		.10	.12	.14	.12	.12		

Variation in Inorganic Solid Content after Administration of Pilocarpine.

Chart 12A.



Variations in Inorganic Solid Content after Administration of Pilocarpine.

VARIATIONS AFTER ADMINISTRATION OF ATROPINE.

The same methods ~~that~~ were used with the atropine experiments as in the case of pilocarpine,- a normal sample was collected during the first period, the atropine taken, and the collection continued.

Volume:- The usual decrease in the volume of saliva secreted was obtained, - Chart 13A, - the maximal effect of the drug usually occurring about the sixth period, toward the end of the experiment. In some of the experiments there was not enough saliva secreted in the fifth and sixth periods for analysis. In one experiment, No. 7, there was a marked increase in volume in the third period, before the characteristic atropine fall. This variation, I believe, was due to an increase in the strength in the stimulation from the chewed paraffine, and not to any drug effect.

Amylolytic Power:- Chart 14A shows the amylolytic power of the saliva to be markedly diminished, the maximal decrease usually occurring about the second period after administration of the drug. In the majority of the experiments there seems to be a tendency for the amylolytic activity to increase towards the fifth or sixth periods, as though the drug effect had worn off. That the atropine is still acting, however, is shown by comparison of Charts 13A and 14A. It will be seen here that, although the amylolytic power has returned to almost nor-

mal, the volume secreted is still on the decline, thus showing that the drug is still acting.

Content in Solids:- There is a marked decrease in the amount of total solids secreted after atropine, the quantity diminishing steadily as the experiment progresses. The percentage composition of total solids is decreased also, but on the whole, to a somewhat lesser degree than the amount secreted. In some of the experiments, however, the decrease in amount and percentage composition is practically parallel.

A glance at Chart 17A of the variations in inorganic solids, shows both the amount and percentage composition of the inorganic constituents to be approximately constant, so that the decrease in the total solids must be due to a diminishing of the organic constituents. This is shown by Chart 16A, both the amount and percentage of the organic solids decreasing in practically the same curvesas those of the total solids, - Chart 15A. In Experiments 4 and 5 the amount and percentage of organic constituents were still on the decline at the end of the period of secretion, while in some of the others the content is more nearly normal about the sixth period.

Summary of Effect of Atropine:- I have shown in the above the well known decrease in the volume of saliva secreted after atropine, and also, that the drug has a retarding influence upon the formation or secretion of the other constituents which were considered, i.e., ptyalin and the content in solids.

To just what physiological action of the drug these variations are due, is a question to be determined. Barcroft (37) has shown that atropine exerts a marked influence upon the oxygen intake of the salivary glands, and Matthews (35) (36) results already refered to, point to the fact that atropine retards the oxidative decomposition of protoplasm. It seems probable, therefore, that the diminishing which I have shown in the secretion of the of the above constituents of the saliva after atropine, is due to a retarding of the oxidative metabolic processes which take place within the secretory cells. The exact point of action of the drug is immaterial; the retarding influence may be effected through the secretory nerve endings, or by direct action upon the gland cells.

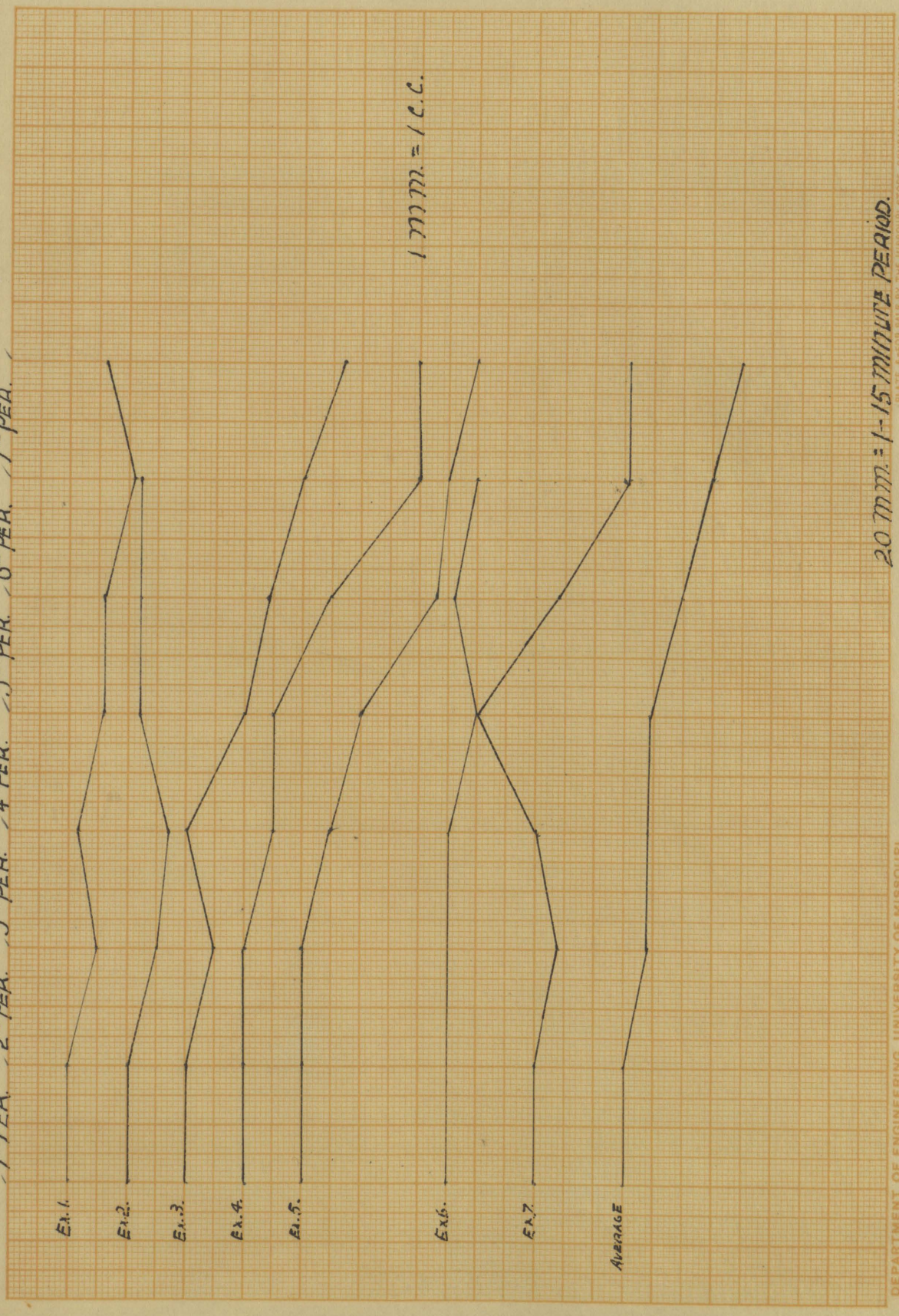
Table 13.

Volume in c.c., samples collected in consecutive 15 min. periods, drug taken between periods 1 and 2.

Exper. and Coll.	Control Per. 1	Pilocarpine.	Per. 2	Per. 3	Per. 4	Per. 5	Per. 6	Per. 7
1. E.	38 cc.	.5 mg	32	35	32	32	26	30
2. E.	38	.5	32	31	35	35	36	
3. E.	45	1.	40	45	35	33	25	18
4. G.	55	.5	55	50	50	40	25	25
5. G.	40	1.	40	35	30	17	15 25	10
6. E.	20	1.	20	20	15	19	15	
7. E.	35	1.	30	35	40	37	15	15

Variations in Volume after Administration of Atropine.

Chart 13A.



Variations in Volume after Administration of Atropine.

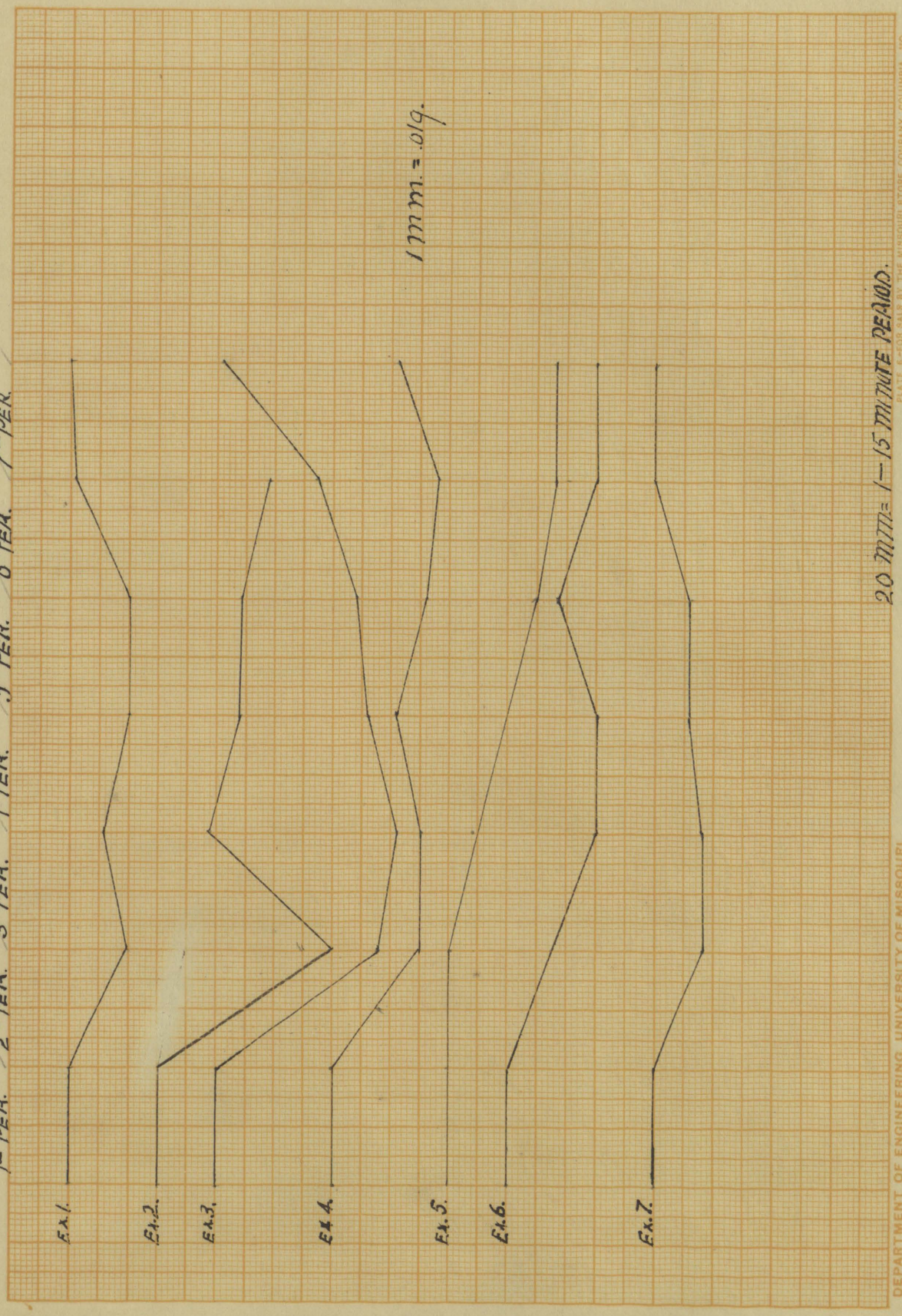
Table 14.

Grams Maltose produced,- samples collected in consecutive 15 min. periods,- drug taken between periods 1 and 2.

Exper. and Coll.	Control Per. 1	Atropine taken.	Per. 2	Per. 3	Per. 4	Per. 5	Per. 6	Per. 7
1. E.	.500 g	.5 mg	.410	.442	.425	.410	.495	.500
2. E.	.638	.5	.335	.495	.469	.469	.425	
3. E.	.741	1.	.469	.442	.500	.522	.605	.756
4. G.	.460	.5	.315	.323	.359	.302	.277	.359
5. G.	.575	1.	.575	.522	.460	.410	.389	
6. E.	.348	1.	.250	.191	.194	.273	.191	.194
7. E.	.273	1.	.198	.198	.201	.212	.261	.261

Variations in Amylolytic Power after Administration of Atropine.

Chart 14A.



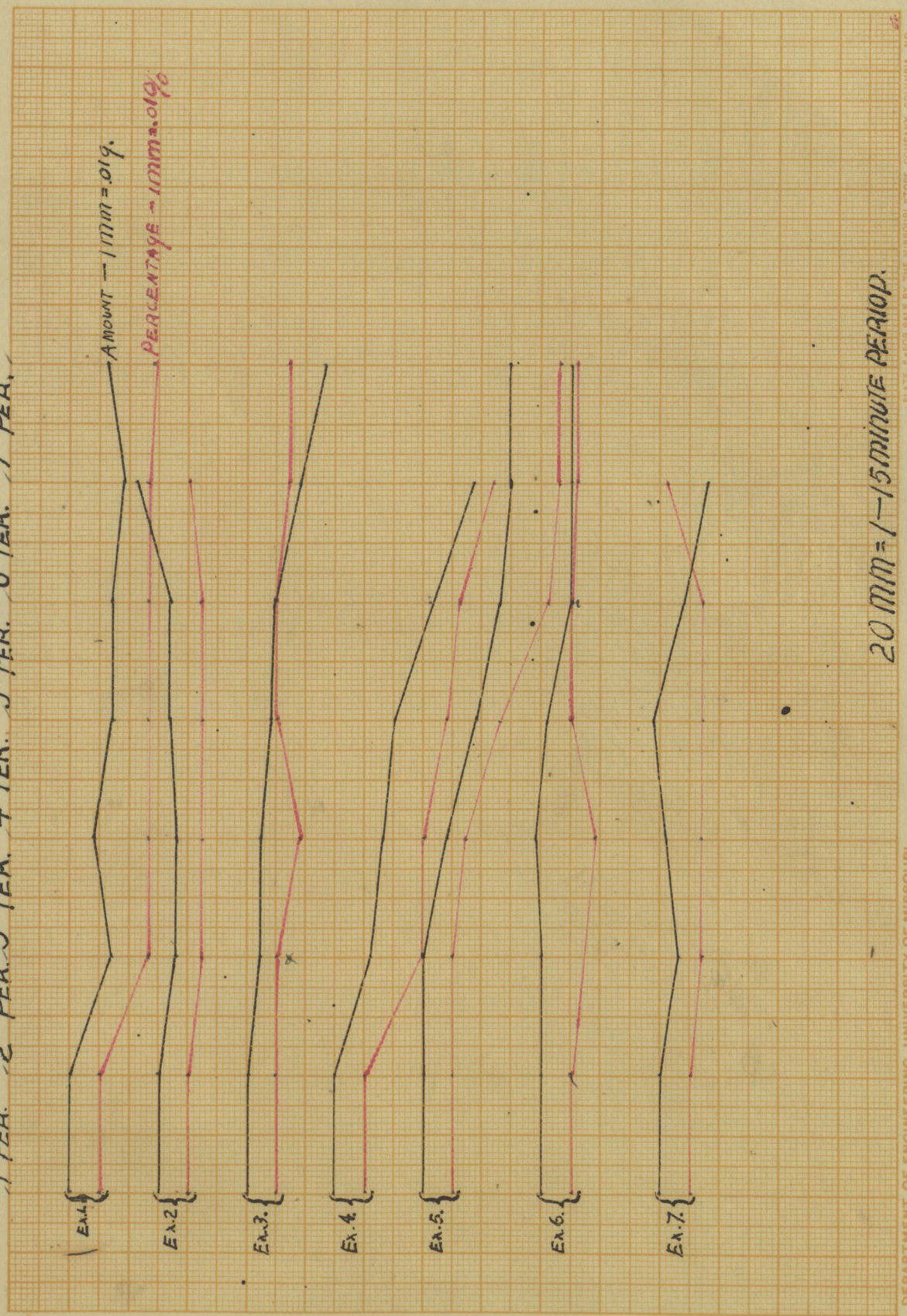
Variations in Amylolytic Power after Administration of Atropine.

Table 15.

Exper. and Coll.	Total solids	Samples collected in consecutive 15 min. periods, drug taken between periods 1 and 2. Control Per. 1	Atropine.	Per. 2	Per. 3	Per. 4	Per. 5	Per. 6	Per. 7
1.	Amt. Sec.	.182	.5 mg	.128	.140	.128	.128	.109	.120
E.	Pctg.	.48		.40	.40	.40	.40	.42	.40
2.	Amount	.167	.5	.134	.130	.147	.147	.202	
E.	Pctg.	.44		.42	.42	.42	.42	.44	
3.	Amount	.207	1.	.184	.189	.161	.151	.110	.079
E.	Pctg.	.46		.46	.42	.46	.46	.44	.44
4.	Amount	.363	.5	.308	.280	.260	.200	.120	
E.	Pctg.	.66		.56	.56	.52	.50	.44	
5.	Amount	.264	1.	.264	.224	.174	.085	.072	
G.	Pctg.	.66		.66	.64	.58	.50	.48	
6.	Amount	.092	1.	.092	.105	.092	.069	.069	
E.	Pctg.	.46		.44	.42	.46	.46	.46	
7.	Amount	.154	1.	.126	.147	.168	.113	.072	
E.	Pctg.	.44		.42	.42	.42	.42	.48	

Variations in Total Solid Content after Administration of Atropine.

Chart 15A.



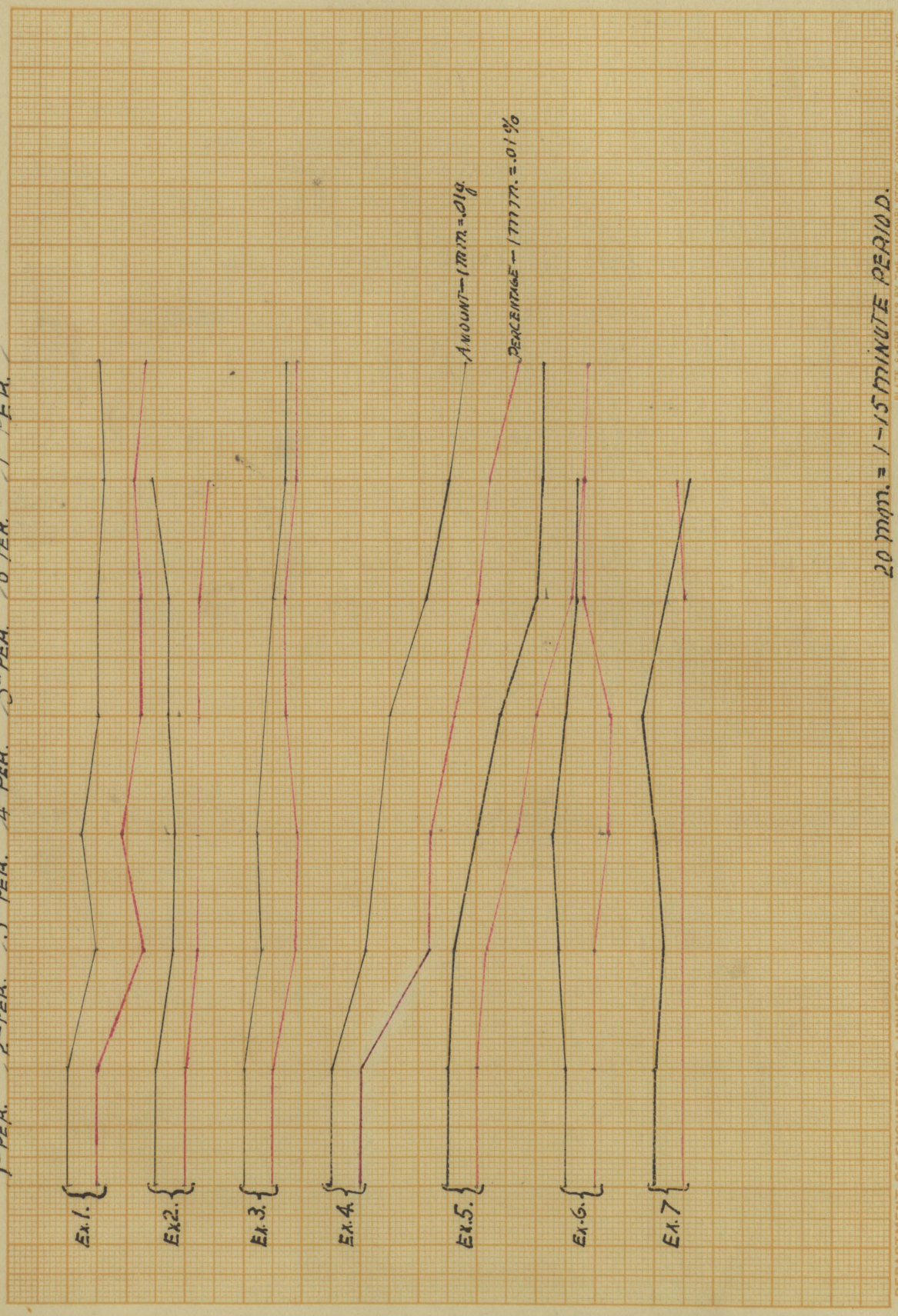
Variations in Total Solid Content after Administration of Atropine.

Table 16.

Exper. and Coll.	Org. Solids	Control Per. 1	Atropine.	Per. 2	Per. 3	Per. 4	Per. 5	Per. 6	Per. 7
		Samples collected in consecutive 15 min. periods, drug taken between periods 1 and 2.							
1.	Amt. Sec.	.136 g	.5 mg	.089	.112	.089	.088	.078	.084
E.	Pctg.	.36		.28	.32	.28	.28	.30	.28
2.	Amount	.136	.5	.108	.105	.119	.119	.147	
E.	Pctg.	.36		.34	.34	.34	.34	.32	
3.	Amount	.144	1.	.112	.126	.105	.099	.070	.054
E.	Pctg.	.32		.28	.28	.30	.30	.28	.30
4.	Amount	.286	.5	.220	.200	.180	.128	.085	.065
G.	Pctg.	.52		.40	.40	.36	.32	.30	.26
5.	Amount	.192	1.	.184	.140	.114	.054	.045	
G.	Pctg.	.48		.46	.40	.38	.32	.30	
6.	Amount	.068	1.	.072	.08	.064	.057	.057	
E.	Pctg.	.34		.34	.32	.32	.38	.38	
7.	Amount	.105	1.	.090	.105	.120	.081	.048	
E.	Pctg.	.30		.30	.30	.30	.30	.32	

Variations in Organic Solid Content after Administration of Atropine.

Chart 16A.



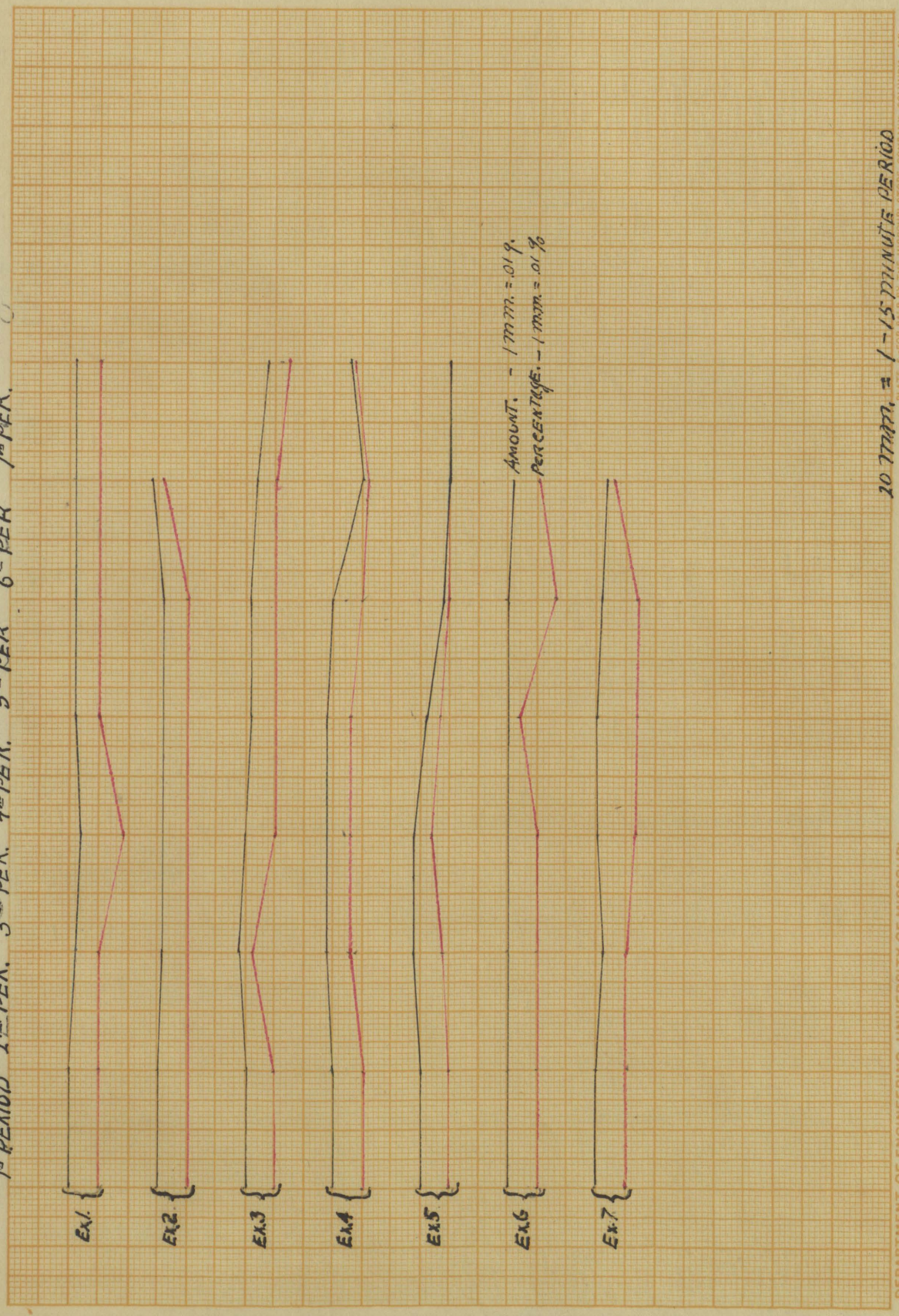
Variations in Organic Solid Content after Administration of Atropine.

Table 17.

Exper. and Coll.	Inorg. Solids	Samples collected in consecutive 15 min. periods, drug taken between periods 1 and 2. Control Per. 1	Atropine.	Per. 2	Per. 3	Per. 4	Per. 5	Per. 6	Per. 7
1.	Amt. Sec.	.045g	.5 mg	.038	.028	.038	.038	.031	.036
E.	Pctg.	.12		.12	.08	.12	.12	.12	.12
2.	Amount	.030	.5	.025	.024	.028	.028	.043	
E.	Pctg.	.08		.08	.08	.08	.08	.12	
3.	Amount	.063	1.	.072	.063	.056	.032	.040	.025
E.	Pctg.	.14		.18	.14	.16	.16	.16	.14
4.	Amount	.077	.5	.088	.080	.080	.072	.035	.040
G.	Pctg.	.14		.16	.16	.16	.18	.14	.16
5.	Amount	.072	1.	.08	.084	.060	.030	.027	
G.	Pctg.	.18		.20	.24	.20	.18	.18	
6.	Amount	.024	1.	.020	.025	.028	.012	.012	
E.	Pctg.	.12		.10	.10	.14	.08	.12	
7.	Amount	.049	1.	.036	.042	.048	.032	.024	
E.	Pctg.	.14		.12	.12	.12	.12	.16	

Variations in Inorganic Solid Content after Administration of Atropine.

Chart 17A.



Variations in Inorganic Solid Content after Administration of Atropine.

THE AMYLOLYTIC POWER.

In the preceeding tables and discussion, only the relative amylolytic power of the saliva after administration of atropine or pilocarpine, as compared with that of the normal secretion, has been considered.

The same amount of saliva, 5 c.c., was used in each digestion and the amount of maltose produced, determined. As has been shown, the changes were very great, the results indicating that either the activity of the ptyalin was diminished, or, what is more probable, that the actual amount of the enzyme secreted was decreased.

In what way both atropine and pilocarpine, which exhibit a mutual antagonism, cause this decrease in amylolytic power, must be determined.

Besides the question of relative amylolytic power, i.e., - the amounts of maltose produced by the same quantities of saliva, - there is another point to be considered. In the case of a drug like pilocarpine, which increases the volume of saliva secreted to such an enormous extent, would not the amount of maltose produced by the total volume secreted in a given period, be greater than that produced by the normal saliva secreted in the same length of time, although the relative amylolytic power of the drug saliva is less than that of the normal secretion? To determine this point, I calculated the amounts of maltose produced by the total volumes of saliva secreted in the various fifteen minute periods after administration of pilocarpine, and

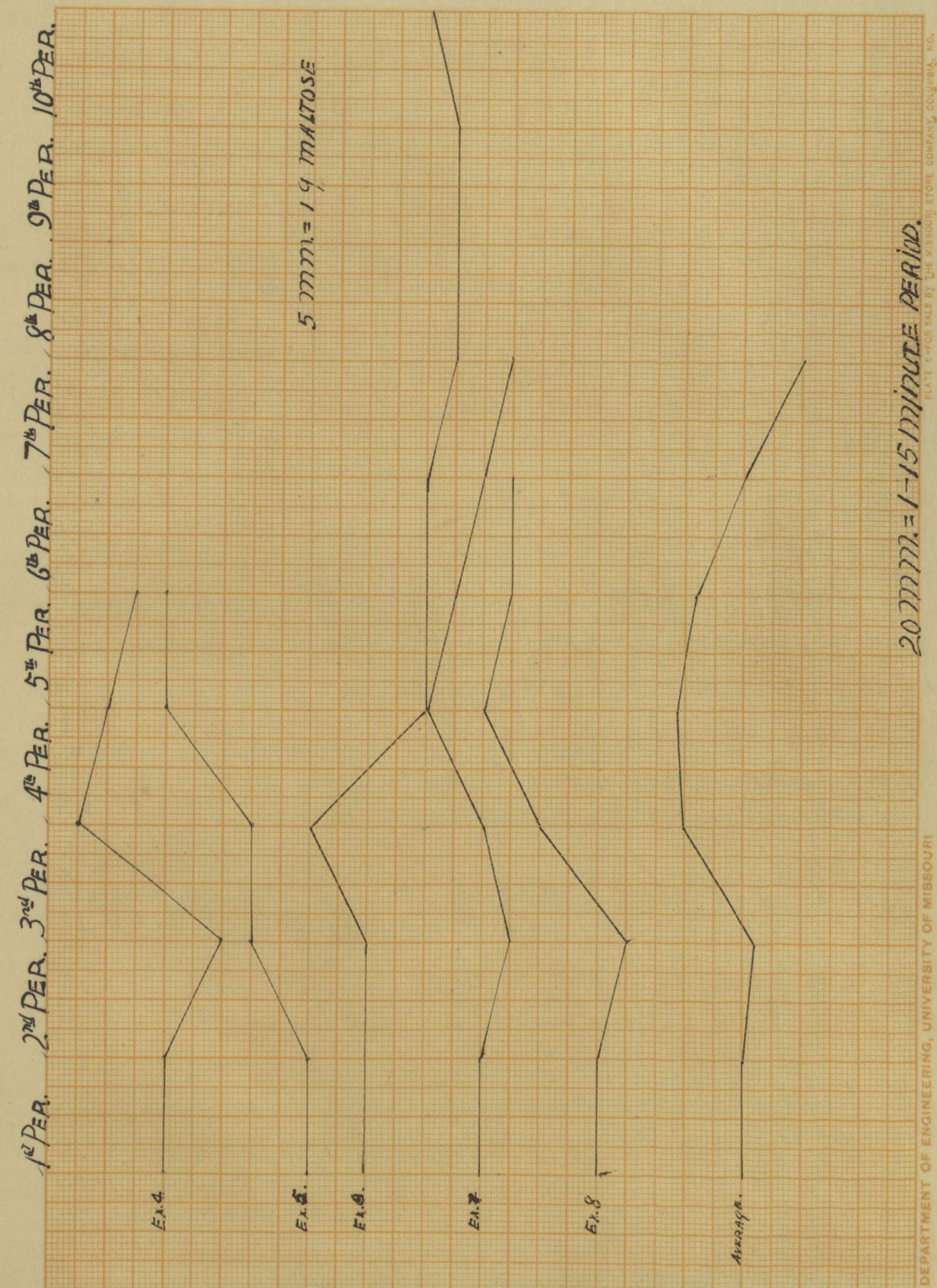
Table 18.

Exper. and Coll.	Grams maltose produced by total volumes of saliva collected in the respective 15 minute periods. Control Per. 1	Pilocarpine	Per. 2	Per. 3	Per. 4	Per. 5	Per. 6	Per. 7
4. E.	4.10	.005 g	2.46	7.06	6.73	5.74		
5. E.	2.91	.01	4.23	4.59	7.18	7.66		
6. G.	5.00	.01	5.40	7.30	3.41	3.28	2.29	2.57
7. E.	3.27	.01	2.22	3.82	5.02	4.59	3.35	2.29
8. E.	4.05	.013	3.28	6.44	8.62	7.01	7.52	

Variations in Actual Amount of Maltose Produced by the Total Volumes of Saliva Secreted after Administration of Pilocarpine.

N.B. The above figures are the amounts of maltose which would be produced by the total volumes of saliva collected in the various 15 minute periods. The results in Tables 8 and 9 were used as a basis for calculation.

Chart 18A.

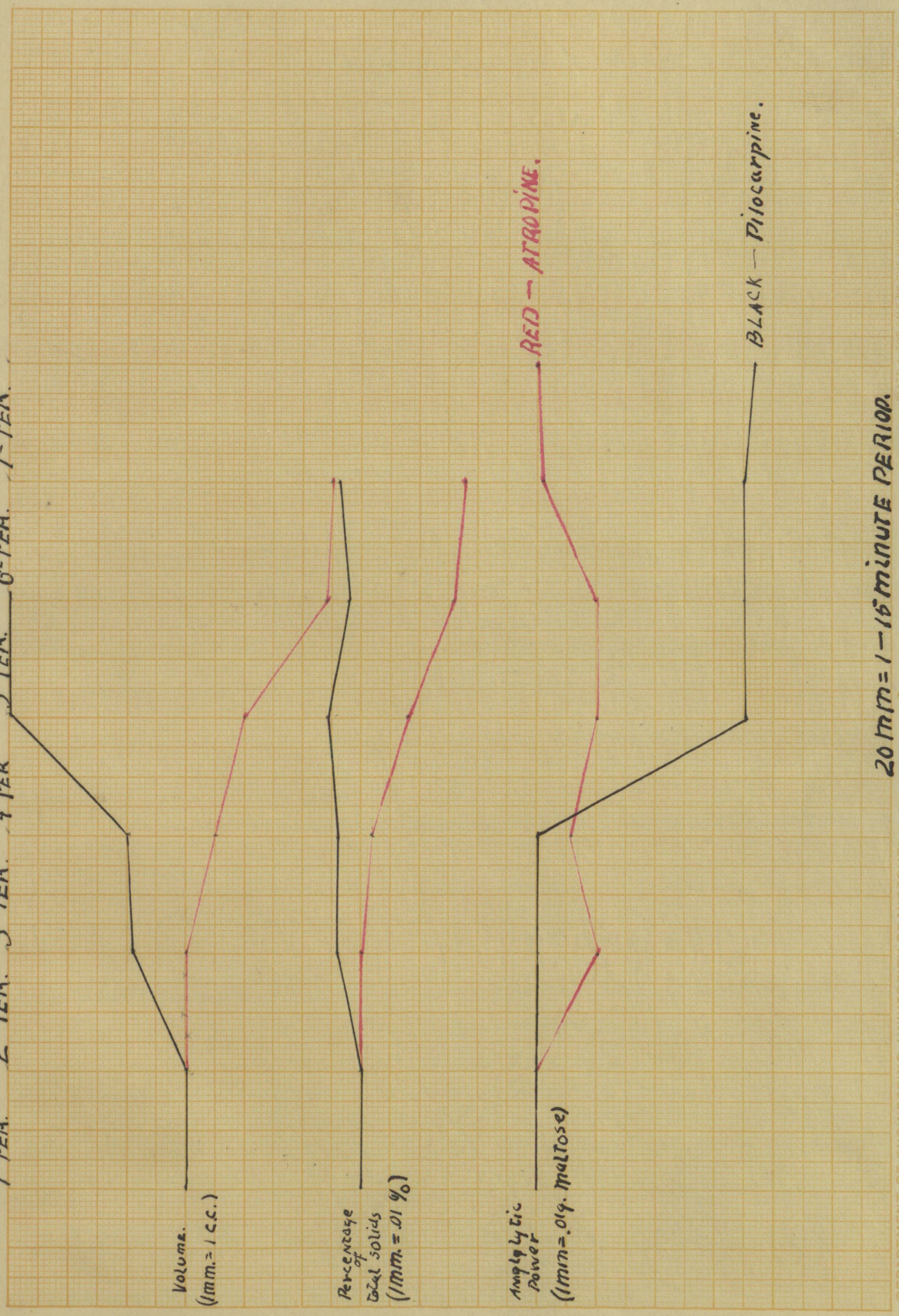


Variations in Actual Amount of Maltose Produced by the Total Volumes of Saliva Secreted after Administration of Pilocarpine.

compared the results with the maltose produced by the total volumes of the normal saliva secreted in the control periods. The figures in Tables 8 and 9 are used as a basis for the calculations.

The results in Table 18 and Chart 18A show that the total amount of ptyalin, as measured by the quantity of maltose produced by the total volumes of the saliva secreted in the various fifteen minute periods, is greater after pilocarpine than in the normal saliva. In other words, although there is less ptyalin in a given quantity of saliva after administration of the drug, than in the same amount of the normal saliva, the increased volume of the secretion caused by the drug, more than compensates the diminished formation or secretion of the enzyme. Of course, unless the effect upon the volume is well marked, this compensation does not occur. In the case of atropine where not only the amount of ptyalin, but also the total volume of the saliva secreted, is diminished, this question of the maltose produced by the entire quantity of saliva secreted during the period need not be considered.

Chart 19.



Summary of Effects of Pilocarpine and Atropine.

SUMMARY.

The above results, I believe, are what would naturally be expected when working with two sets of drugs as atropine and pilocarpine. Atropine exerted an inhibitory influence upon the formation or activity of all the properties of the saliva which were considered. Pilocarpine, with the exception of its effect upon the amylolytic power of the saliva, had a stimulating action upon the formation of these same components.

The fact that the two drugs have opposite effects upon the other properties of saliva, while both decrease the amylolytic power, though to a different degree, brings out the point already mentioned, - that the secretion of ptyalin seems to be entirely independent of the formation of any of the other components of the saliva.

I have already shown that the amylolytic power has no definite relation to the volume secreted. The additional fact that the amylolytic activity is diminished, both when the solids are increased and decreased, justifies this conclusion.

The action of atropine and pilocarpine upon the amylolytic power seems also to be of different duration from the effect upon the other properties of the saliva. In many of the experiments with both drugs, the amount of maltose produced is up to normal, while the volume and percentage of solids still show great variations.

From my results on the variations in percentage and amount of solids in the saliva, and granting that the action of these drugs is upon the nerve endings, it appears that atropine and pilocarpine affect both the "trophic" and "secretory" fibers; the former paralyzes,and the latter stimulates them. (In speaking of "trophic" and "secretory" fibers, I mean simply the factors which influence the formation of the "trophic" and "secretory" elements proper, of the saliva).

One point I noticed in connection with my experiments with atropine appears to be at variance with some results of other investigators. Carlson, Greer, and Becht, (14), concluded that a diminished oxygen supply increase the solids of the saliva, and Barcroft (37) showed that after atropine paralysis, stimulation of the chorda caused no increase in the oxygen intake, although there was a great increase of the carbon dioxide output.

My results, however, show that atropine diminishes the percentage of solids reflexly secreted, whatever may be the variation in the oxygen supply. Of course, Barcroft results may not mean that the oxygen supply is actually diminished after atropine, but is simply not increased upon stimulation of the nerves to the gland.

It will be remembered, of course, that only therapeutic doses of the atropine and pilocarpine were taken, but as the smallest and largest doses cause practically the same variations, I believe that my results are characteristic of the physiological effects of the two drugs.

CONCLUSIONS.

1. The volume, amylolytic power, amount and percentage composition of solids secreted, of normal saliva, remains approximately constant during a continuous period of secretion lasting for six or eight fifteen minute periods. If there is any change, it is a very slight falling off of the percentage composition of organic solids, and at times of the amylolytic power.

2. Pilocarpine reduces the amylolytic power of the normal saliva from thirty to sixty per cent.

3. Pilocarpine increases the amount and percentage of both the organic and inorganic solids of the saliva; the greatest increase is in the organic constituents, however, The percentage increase of the solids is not nearly so great as the increase in the actual amount secreted.

4. Atropine diminished the amylolytic power of the saliva from about fifteen to thirty per cent.

5. Both the amount and percentage composition of total solids secreted are greatly diminished by atropine. The decrease is almost entirely in the organic constituents.

6. Pilocarpine and atropine affect the factors which influence both the "trophic" and "secretory" elements of the saliva.

7. The effect of atropine and pilocarpine upon the secretion, or activity of the ptyalin of the saliva, bears no definite relation to the action of these drugs upon the other physico-chemical properties of the secretion.

8. Although the relative amylolytic power of the saliva is much diminished by pilocarpine, the amount of maltose produced by the total volume of saliva secreted in a given period, after administration of the drug, is greater than that produced by the normal saliva secreted in the same length of time. This is due to the increase in the volume of the secretion caused by the pilocarpine.

I desire to thank Dr. R. B. Gibson, who has aided and directed me in my work throughout the year.

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