The Trustworthiness
of the present-day preparations
of the Digestive Ferments,
as tested experimentally and clinically:
with some introductory comments upon
the recent physiology
connected with the subject.

A Thesis written for the M.D. degree
of the University of Edinburgh
(1894)
by Edmund Moody Smith,
M.B., C.M., Edin.,
Whitwell House, Scarcroft Rd., York.
April 25, 1894.
Declaration

To the Dean, and Faculty of Medicine of the University of Edinburgh.

I, Edmund Moody Smith, of Whitewell House, Scaracroft Rd, York, formerly of Bradford, Bachelor of Medicine and Master in Surgery of the University of Edinburgh, do hereby (Thesis attached) apply for the Degree of Doctor of Medicine of the University of Edinburgh, upon the "old Regulations", existing at the time of graduation as M.B., C.M. in the year 1888.

I do hereby declare the accompanying thesis, upon "The Trustworthiness of the present-day preparations of the Digestive Ferments", to be entirely my own unaided work and composition; and I further wish to declare that the work it records has not been, in the slightest degree, connected with business interests of the firms mentioned therein, nor have I received any remuneration whatever for giving them and their productions mention therein.

I have also to declare hereby:

That I am 30 years of age;
That I graduated M.B., C.M. Eden: Univ: August 1888, and was duly registered as such, August 1888;
That my name, with alteration of address, is still on the Register;
That since my graduation in 1888 I have been constantly engaged in general medical and surgical practice; (Certificate attached)
That, in accordance with existing regulations, I
have passed the Preliminary Examination in General Education of the University of Edinburgh in Greek, Logic, and Natural Philosophy, and in French. (Certificates are herewith enclosed).

As witness my hand,

Edmund W. Smith, M.D. Cant. Univ.

To the Dean and Faculty of Medicine, Edinburgh University:

I do hereby beg to apply, through the accompanying Thesis, for the Cameron Prize, 1894, in Therapeutics, and also for the Milner Potterjill Gold Medal Award of 1895— as my Thesis is an essay on a Therapeutical and Practical subject, and embodies an original research. I crave the pardon of the Faculty if these applications be, in any manner, out of order, but humbly beg to lay my claims before the Faculty.

I have the honour to be, Gentlemen,

Yours faithfully,

Edmund W. Smith
Thesis.
The Futility of the present-day preparations of the Digestive Ferments, as tested experimentally and clinically: with some introductory comments upon the recent physiology connected with the subject. By Edmund Moody Smith, M.B., C.M., Edin.

There are three or four reasons for making a special study of this subject at this time:—(1) the great amount of dyspepsia which, as practitioners, we are called upon to treat; (2) the value of the Digestive Ferments preparations in the treatment of dyspepsia and of all febrile conditions of the digestive organs, their superiority, indeed, in so many cases where the administration of alkalis, bismuth, or other alteratives, medicines, fail, or only give transient relief, and where prescribed dietaries are either insufficient, or but ill-attended to; (3) the immense number of the preparations of the digestive ferments, of various kinds, and by so many different makers, advertised and otherwise brought to our notice.

This last reason, (3), has led me to inquire experimentally, and to some
extent, clinically, how far these many preparations of to-day come up to requisite and recognised standards. There have been many and eminent workers in this field already, to whom had occurred the same kind of inquiry, and very valuable their researches have been, but as no further investigations have been made to my knowledge during the past ten or twelve years, it seems legitimate now to ask, Are the older preparations still made perfectly trustworthy? And are the numerous new preparations equal to required standards? The researches of twelve or more years ago tended to shake the general faith of the profession in the large majority of these preparations, and considerable loss of reputation have "piping", its allies suffered since; but that they have done good is evident from the vast improvement in the preparations of the present day. It appeared to me that I might render some small service to my fellow-practitioners, and perhaps to the whole profession, if my observations could assure them that there are now many preparations
that are trustworthy and highly commendable.

Such an assuring investigation appears the more desirable, when one takes into consideration the increasing amount of dyspepsia due to the hurriedness of business, and of educational competition, — long intervals between meals; irregular mealtimes; scrappy, sloppy, meals taken hurriedly in "stuffy" workshops; absurdly short hours for meals, with previous and subsequent hasty walks to and from home & workshop; hard mental studies continued during and immediately after meals, as so common in "exam"-work; prolonged mental strain, anxiety, and depression; excessive and indiscriminate use of tea and other stimulants by mental workers,—to say nothing of decayed teeth, bad dentistry (quackery), errors in diet, limitations of diet, insufficient use of fish, fruit, and vegetables by the poorer classes, etc.

I have made a large number of experimental observations upon the various present-day preparations of the digestive ferment, not as laboratory research scholar, who spends most of the day at his
particular work, and is never, or rarely called away therefrom, but as a general practitioner, not having more than one, or at most two, hours to spend at each set of experiments, and these of course liable to interruptions. I have worked with the simplest apparatus, but sufficiently accurate for my purpose, not attempting to make fine, prolonged, analytical observations of a quantitative character, — but I venture to claim that perhaps, to the clinical observer, workman, there have been none the less serviceable — As practitioners, we do not demand, I think, preparations capable of doing the almost fabulous work some of them claim to do. If they satisfactorily meet the recognized requirements, if they prove experimentally trustworthy and clinically practicable — I opine that these are sufficient qualifications for the prescriber. This is the standard by which I have tested all the many preparations I have dealt with, not attempting to go far towards verifying claims as to extraordinary powers. My experiments, therefore, have been chiefly short-time experiments, but of a time
as long as is required by the British Pharmacopoeia official standard, and as long as necessary in order to test real value and trustworthiness. Many of the pepsins and pancretins, put forth by the minor makers, prepared avowedly according to B. P. Recipes, have been repeatedly proved to be valueless, or nearly so; I have limited myself to the well-advertised products only.

Before speaking of my experiments, and of observations connected therewith, there are certain points connected with the recent physiology of the subject that call for some comment.

In the act of mastication the food is well mixed with the saliva, which normally is alkaline. The active constituent of the Salivary Secretions is the ferment called Ptyalin (which occurs in the proportion of 139 per cent); its function is to convert about 50 per cent of the starchy foods into Dextrose and Maltose, % some portion into Glucose, along with the production of some lactic acid. Digestion of the starch granules is the first stage of the conversion process,
and this stage is effected within a few minutes. The presence of alkali in the saliva is not absolutely essential to the action of the Ptyalin, as experimentally, it has been proved that it can act well in neutral, and even slightly acid conditions; indeed it acts in the presence of the lactic acid produced in the course of the digestion of starch. Further, M. F. Arnold Lee (British Medical Journal, 1880) asserts that the action of Ptyalin is not hindered by the presence of peptin, along with small proportions of either lactic acid, or hydrochloric acid. Griswold denies this statement, but my own experiments prove it, and the general opinion of recent physiology is to the effect that the starch-conversion processes continue after the food has entered the stomach, until the stomach contents become too acid, (5 per cent has been fixed in McIndoe's physiology), when its action ceases, i.e. after one or 1½ hours. The work of Ptyalin is completed by the Amylase of the pancreatic secretion. It will be more convenient to speak further discuss
the digestion of starch when dealing with the pancreatic secretion.

Ptyalin can be separated from the salivary secretion by the following methods:

(1) To some saliva, add phosphoric acid; then add lime water until quite alkaline, result = a precipitate of Calcic Phosphate carrying down the Ptyalin; then wash this precipitate after filtering, remainder is a solution of Ptyalin, add alcohol, we get a white precipitate of Ptyalin, which is dissolved in water, precipitated again, & dissolved again, or evaporated to dryness, as required.

(2) Or digested minced-up salivary glands in absolute alcohol for 24 hours; evaporate to dryness, and then place the glands in glycerine for several days; the Ptyalin is then precipitated from this glycerine extract by alcohol, & dried.

(3) Sir W. Roberts extracts Ptyalin from the salivary glands (freshly obtained) with Chloroform water, or with dilute alcohol, or with dilute Boracic Solution.
It is now generally admitted that there are two ferment in the gastric juice, — Pepsin, a peptone-former, and a milk-curdler, which may be called the Gastric Rennin. This latter, unlike the Pancreatic Rennin, can act in the presence of acid, and yet quite apart, also, from acid, which curds milk, of course, in any case. Commercial Rennet is a bine extract of the gastric rennin of the calf. Bine is fatal to pepsin; however, so that a bine extract contains only the rennin active. This rennin evidently coagulates some portions of the cascin that are partially or wholly digested, afterwards by pepsin. There are other differences from the pancreatic Rennin which will be mentioned hereafter.

Notwithstanding much doubting experiment and discussion, it still remains the proven fact, that pepsin can convert proteids into peptones only in the presence of free hydrochloric acid, which occurs in the gastric secretion in about the same proportion as pepsin, viz. about 3 per cent. If pepsin be used alone, without hydrochloric acid, the result after prolonged digestion, is only
an intermediate body, called pepsin. It has been proved, by many observers, that hydrochloric acid is the one constant and essential acid occurring in the gastric juice and in gastric digestion, although it would appear that other acids produced during the process of gastric digestion are also conducive thereto, and to the action of pepsin. Some of the hydrochloric acid unites with bases of organic salts of the foods ingested,—with the acetates, lactates, malates, etc,—and liberates their organic acids, which play a further part in the gastric digestion. So say Mr. T. Arnold Lee, and other observers.

The hydrochloric acid also appears to some extent, to form salts with leucin and tyrocin,—substances formed in greater or less degree during digestion,—and with the slight quantities of phosphates occurring in the gastric juice, for solutions of albumen have been experimentally digested by:

(a) Pepsin with leucin hydrochlorate,
(b) Pepsin with calcic lactophosphate,
(c) Pepsin with denin, tyrocin, calcic
lactophosphate, and common salt, all mixed. (Arnold Lee)

It may thus be surmised that the union of hydrochloric acid with these top-products of digestion is perhaps one of the ways in which hydrochloric acid acts as an indirect antiseptic in the stomach, carrying them off in this utilitarian fashion. Hence also the rationale of the administration, by many physicians, of dilute hydrochloric acid, in cases of dyspepsia. Where there is lactic and butyric fermentation, where septic changes occur markedly, Pepain, of itself, is not an antiseptic; this has now been repeatedly proved.

The free hydrochloric acid of the gastric secretion has its origin in the sodium chloride of the surrounding bloodstream. Maly says that lactic acid is the decomposing, or liberating agent, but the peculiar vitality of the gastric gland-cells is a much more probable agent. (Landois' physiology) - Pepain appears to be preceded in the gland-cells by an inactive, powerless, precursor body,
called pepsinogen, from which the pepsin has to be liberated (possibly by the hydrochloric acid), before any digestive activity appears. Peptones are very soluble, easily diffusible, uncoagulable. If a solution of a digested proteid be filtered and evaporated to dryness, we have a glassy, straw-colored residue like dried gum. This is peptone. It chips off in shining scales, and can be reduced to a fine, white, hygroscopic powder; it is not in the least viscous. As it dries, crystals of leucin and tyrosin can be observed, and these are evidently the results of the splitting of peptones, i.e., variable, ultimate products of proteid digestion and conversion. Sir Wm. Roberts (dunleian lectures, 1880), and others, have experimentally proved that peptones are absorbed and assimilated, and that they can, of themselves, support life, and increase body weight. That this is true, a severe case of enteric fever, in my own recent experience, has very prettily demonstrated; peptonized milk, cocoa, meat-juices, making the convalescent stage a shorter.
period of rapidly regained strength, and flesh, and general tone.

It is interesting to learn from Sir Wm. Roberts' deeply interesting Lumleian lectures, aforementioned, that the action of Pepsin is not antagonized in the least, by 1 per cent of either Salicylic Acid, of Quinine, or of Borax. But it is hindered by Excess of water, excess of acids, and by alkaline salts, alum, tannin, and other astringents.

Another important fact about the action of Pepsin, so far as Experiments show, at any rate, is that it always requires a comparatively large amount of water in order to effect a complete digestion. This latter fact is strikingly borne out in many of the usual experiments with pepsin. The beaker has to be constantly agitated so that the peptones, as they are formed, do not become too concentrated around the remaining undissolved albumen, of the digestion of which would thus be considerably hindered, that even an insoluble combination of the solid protid and peptone occurs. Hence a large quantity of water is required for
Artificial and Natural Digestion.—Twenty years ago Kühne pointed out that the conditions of digestion in the alimentary canal differ considerably from the conditions that exist in the usual artificial digestion experiments in flasks or test tubes.

These conditions are:—firstly, the constant movement of the food mass in the intestine; secondly, the constant removal of digestive products; and thirdly, the constant renewal of digestive fluid. All these points are difficult of attainment in the laboratory. Dr A. Sheridan Lea publishes in the Journal of Physiology, March, 1890, results of some experiments on artificial digestion, in which he seems to have more nearly imitated natural conditions than has previously been the case.
His apparatus consisted of a glass vessel (a) about 2 ft. high and 6 in. wide, with three tubulures (b, c, d.) This was connected with a copper vessel (A) filled with water, and heated to any temperature by a burner (c). A current of water could be made to flow through the coil of pipe in (a) entering as shown by the upper arrow. The warmed water flowed into (a) at the tubulure (b), filled it, and flowed out at (c). By regulating the burner and the rate of the flow of water through the coil, a constant temperature of 40° c. could be easily obtained. Immersed in (a) was the cylindrical glass vessel (g) whose lower end was closed by a cork through which passed the tube (h), the lower part of which was of India-rubber, and passing through the tubulure (d) was connected with the glass tube (h). Thus any fluid could be placed in (g) and kept at the temperature of the water in (a), and by lowering (h) the contents of (g) could be drawn off when required. A loop of special parchment paper tube, as used by Kühne for dialysis experiments, was suspended in (g), and connected by the string (k) to a motor by which any desired rate or extent of up and down motion could be communicated to it.

In use, the substance to be digested was placed inside the dialysing tube (i) together with the digestive fluid, (g) was filled with fluid similar to that inside (i) but without ferment, and the contents of (g) and (i) maintained at any desired temperature by means of the current of warm water flowing through (a). Finally the dialysing tube was kept in constant motion by the string (k).

This apparatus, it will be seen, secures at all events an approximation to two of the more important conditions of sound digestion, viz., continuous movement and removal of digestive products. The motion and the mixing produced by it are good, but the removal of digestive products depending as it does on their diffusibility, falls far short of natural conditions, governed as these appear to be by a special selective activity of the intestinal epithelium even more than by the physical properties of the substances to be absorbed. However, this appears to be very efficient as a dialyser, and much superior to other forms for a similar purpose.

Is it not probable that the gastric glands keep up a constant outpouring of their secretion during the digestion of proteids in the stomach, and, in this way, compensate for want of sufficient water ingested? Much liquid (over one pint is stated to be excessive) along with food is not desirable at all times, with all people, and under all circumstances. A diminished quantity of water ingested along with proteid food, would be compensated by the slow, continued
outpouring of secretion in the stomach, whereas, in experiments, one has to
provide a comparatively large quantity of water from the very beginning of the
digestion process. There seems to be very much wisdom infairchild's recommendation
that prepared peptones are best administered
in small doses, repeated several times
between each meal, instead of in one
full dose taken just before, with, or
soon after a meal. This method is an
imitation of the natural method of the
stomach, in keeping pace with the
absorption of the peptones, and as far
as I have tried it, it answers very well.

The duties of the stomach may be
summarized as follows:—
(a) to digest a certain amount of the
proteid food, and absorb the resultant
peptones.
(b) to curdle a certain amount of milk,
to partially, or wholly, digest the casing
of those curds, and to absorb the
resultant peptones.
(c) to absorb such starchy foods as have been converted into soluble forms of sugars by the salivary ferment.

All fatty food is quite unaffected so far as digestion is concerned, though fats long-detained probably give off butyric acid, one of the causes and constituents of the nauseous emetions of dyspepsia.

The Pancreatic Secretion, it is generally agreed, contains four ferments:
1. Steapsin, a fat-splitter & emulsifier;
2. Trypsin, a peptone former;
3. Rennin, a milk-curdler;
4. Amylopsin, the ferment which completes the conversion of starch-yords into the assimilable forms of sugar.

The action of Steapsin has been much debated and remains somewhat a matter of dispute. Most probably, however, it seems agreed, that it effects not "a minute mechanical subdivision of the fat-globules", merely, but a true emulsification of the fatty acids, it has liberated from the neutral fats, into the Sodio Carbonato of the pancreatic juice
and of the bile, combined, or coupled, with an actual saponification. The alkaline, albuminous fluid, milk, has been called "a perfect emulsion." But Sir Wm. Roberts, in his Lumbian Lectures, considers that he has good reasons for asking, does a soluble, emulsive ferment exist at all? Is it not rather a creature of inference, Trypsin being the only one of the four ferments as yet separated? His experiments revealed: (1) that the pancreatic secretion can still emulsify fats after being well-boiled, whereas none of the other ferments can survive a temperature of 160° or 170° Fahrenheit. Is it conceivable that there should be one single ferment, capable of such superior resistance to high temperatures? But, surely, Sir William forgets that boiling does not destroy alkalies, which, as his experiment showed (2), can alone emulsify any fat or which contains, be it ever so little, free fatty acid. The most commonly fatty oils generally do contain the soda carbonate, alone, is sufficient for emulsification, he says. True, but it still remains highly probable that
Trypsin, the pancreatic analogue of pepsin, completes the conversion of proteids into peptones. The researches of Sir Wm Roberts and others as to its modus operandi reveal peculiarly interesting results. Of the two ferments, pepsin and trypsin, the latter digests the cascin of milk much more quickly.
and completely, pepsin leaving a large undissolved residue. But albumen
is much more quickly digested by pepsin than by trypsin, and trypsin
leaves a considerable residue. A solution
of raw egg albumen in water (1 in 10)
does not coagulate on boiling. Raw,
this solution will resist the action
of both ferments persistently, but, after
being boiled, it is digested with readiness.
If this boiled albumen solution be
digested with trypsin (as contained,
say, in a good "pancreatin" preparation),
we find that the process is slow, and,
owing to its flocculency, somewhat deceptive. After 2 or 3 hours, the
process ceases, leaving some quantity
of floating flakes, which are insoluble
in either hot or cold water. But if
we filter off these flakes we obtain a
transparent solution of peptone,
whilst the flakes digest readily with
pepsin and hydrochloric acid. These
flakes appear to be alkali-albumins,
which can only be digested by acid pepsin.

When the bile arrests the action of pepsin,
it precipitates undissolved alkali-albumins
from the solution of peptones, for solution by trypsin.
The presence of alkali does not appear to be absolutely essential to the digestion of neutral solutions of albumen by trypsin, nor to the curdling of milk by the rennin, but it evidently does expedite both processes as my experiments and observations confirm. The alkali also neutralizes the acid chyme, preparatory to their action, and assists in the emulsification of fats.

If trypsin continue to act upon the peptones (or "typtones") it has formed, some part of the peptones (antipeptones) is converted into leucin, tyrocin, hypoxanthin &c., & later on, into indol, skatol, & other fecal products. Hemi-peptones do not so split up (Landais). Fibrin and albumen never swell up in pancreatic juice, as they do in the gastric juice, or, at least, in mixtures of pepsin and hydrochloric acid — they are eroded and dissolved. Trypsin is also said to be preceded, in the pancreas, by a precursor of a passive body called trypsinogen, or zymogen.
Amylopectin differs from the Ptyalin of the Saliva in several points of digestive power. Ptyalin effects nearly all the liquefaction of starch-foods, and commences the sugar-forming conversion-process, but it cannot act at all upon unboiled or raw starch; whereas Amylopectin is able to act upon starch, partially boiled, and, to some extent, even upon raw starch; Amylopectin, therefore, effects the greater part of the digestion of starch, besides, also, producing even still more assimilable forms of sugar.

The digestion of starch, as artificially exhibited by the action of ptyalin, by its analogue, Diastase, by Amylopectin, constitutes a very pretty study, followed carefully, through its several stages. These may be stated briefly as follows:

1. Liquefaction of the gelatinous mass of boiled starch; this occurs in a few minutes.

2. The iodine-test gives a violet reaction, instead of the usual deep-blue colour with starch, indicating the formation of intermediate bodies called starcho-dextrones; Schlink's glucose-test reveals the absence of sugar.

3. Simpler starcho-dextrones are indicated by
the beautiful red reaction with iodine solution; still there is no sugar.

(4) Iodine next ceases to give any colour-reaction with starch, whilst Fehling's solution gives some distinct indication of the presence of sugars; at this stage, the acho-ro-dextrins have developed.

(5) Fehling's solution gives rapidly increasing reactions of sugar (maltose, dextrose, glucose).

It is believed that these acho-ro-dextrins are absorbed, in some quantity as well as the sugars. Glycogen is said to resemble the acho-ro-dextrins in character, like them, can be transformed into maltose and glucose by means of diastase.

According to Professor Rutherford's lectures (1886), the intestinal juice contains a ferment which continues the digestion of starch, and another ferment, confirmed by Sir Wm. Roberts (Linnean Lectures 1880), which converts cane-sugars ingested into dextrose and levulose. Claude-Bernard has asserted that cane-sugars cannot be assimilated except as levulose.

A paper, read at the Pharmaceutical
Conference in 1892, by Mr. Grierson of York, detailed some experiments upon the "Starch-digestion," in which the author had found, that some of the starches, after the usual boiling, long resisted, apparently, the action of both pancreatic essence and malt extract. Such resistant starches were maize, wheat, rice, and wheat flour. These are generally believed to be least digestible; tapioca, arrowroot, potato, and oat starches digesting much more rapidly. This observer could not obtain any results whatever, he said in Conference, with maize &c., but it was pointed out, in the subsequent discussion, that the use of iodine as the sole indicator test, as regarded the conversion of starches into sugars, was somewhat fallacious. The iodine test is so exceedingly delicate in its action upon starch, that if there be any small quantity of starch unaffected by the digesting-ferment, we obtain the characteristic amyl iodide-blue, which may be most persistently reiterated, especially if there be present unboiled granules of starch, with perhaps very resistant
cellulose cuticles (as in maize-starch). These starches need well-boiling before being subjected to crucial artificial digestion. My own experiments very markedly confirm the fallacy of using only the iodine test, and the necessity of using Fehling and other sugar-tests in comparison with it, in order to be just to our results. Moreover, the pancreatic essence (Beasdale's) used in Mr. Grierson's experiments, was one, which, judging by the samples supplied to me, I found to be of only very feeble capacities— the most resistant starch—granules, well-boiled, not too diluted, (not more so, in fact, than so as to produce a stiff jelly, when cooled), subjected to the digestive action of Pancreatin, 1/2 maltines, (otherwise well-proved to be reliable, as by their action upon albumens and more digestible starches), and carefully tested by iodine-solution and Fehling's solution, in comparison, have in all my observations, yielded sooner or later (in two hours at most) to the action of the ferments— An
excellent way of watching the disappearance of starch, as it is formed into sugar, is by first staining it with iodine, the usual deep blue. The blue colour slowly changes, and finally disappears in the manner above described, i.e., through the same gradations, and upon its disappearance, the solution of starch reveals the presence of sugar when the sugar tests are employed—no sugar test being so handy and decisive of course as the Fehling Test (Copper Test). By this method of watching the conversion of starch, however, it is most important to keep the solution neutral, and at a temperature not higher than 95 or 98 °F, as Amyl Iodide is very unstable in alkaline conditions, and at 100 °F.

It need scarcely be noted that the Hepler Malt preparations, and Malts of the best Makers, answer fully experimentally, to all expectations of their starch-digesting capacities.

The pancreatic digestion goes on not only in the duodenum, but also in the jejunum, and upper part of the ileum.
Contribution upon this subject was Dr. Allchin's Radcliffe Lecture (1891) on "Duodenal Indigestion", not only in its bearings upon the physiology of the subject, but upon the rationale of the administration of the various preparations of the digestive ferments. Dr. Allchin's conclusions as to the causes of Duodenal Indigestion may be summarized as follows:

1. Impropriety in quantity or in composition of the Chyme. Under this heading a whole thesis might be written upon "Errors in diet", but such a discussion is not within the scope of the present thesis. But supposing there to be an excess of protein ingested, an excess in relation to the individual's requirements, the result is a greater disparity in the disintegration both of the proteins and of peptones delayed in absorption. More leucin, tyrosin, and other by-products, or ultimate effete products are formed, and disorders of metabolism therefore follow, along with increased risk of putrefaction and of absorption of lensamines. Micro-organisms appear to be present, constantly, in the duodenum & small intestine, but the general consensus of opinion is, also, that these are quite unimportant, except in abnormal conditions.
of digestion, when they are the extremely probably cause of putrefactive decomposition.

An excess of carbohydrate food is often an encumbrance to the stomach. Its presence involves an excess of lactic acid being produced, and this acid delays the insapping and the operation of the hydrochloric acid, which should be quite established before the carbohydrates have been in the stomach 2 hours; it also means the risk of butyric lactic fermentation occurring in the stomach, instead of in the intestine, with consequent sensations into the mouth, as well as probably painful indigestion of the proteins in the stomach.

The intensely sour vomits of dyspepsia — so intense, often, as to "burn" the throat, set the teeth "on edge," and cause smarting of the eyes, — are due to the lactic, acetic, and butyric acids, in excess, formed in the fermentative decomposition of starches & sugars. I am convinced that (as much) more of the dyspepsia, that I have seen, is due to the indigestion of carbohydrates than of proteins, both in excess of that ingested, and to errors in cooking, and in mixing with other foods and with excesses of such liquids as weak or very
strong tea (solutions of tannin)—hence I use the compound preparations, such as lactopeptin, far more than simple peptic preparations.

(2) D. Allchin points out as a second cause of duodenal indigestion, what is similarly true of gastric indigestion, viz.:—some perfection, in quantity or quality, of the digestive secretions—In this case, however careful and correct the dieting, there occurs imperfect peptonization, organic fermentation, excessive production of organic acids & ultimate products, an over-acid chyme, and consequent excessive or premature peristalsis, and destruction of pancreatic ferments. These cases I believe are not uncommon, and call for the administration of pancreatic, or compound preparations of deficient, exaggerated, peristalsis, degeneration, and distension of the bowel hinder absorption, and excessive fermentative changes. D. Allchin is very, very true when he says, that dyspepsia may cause continued dyspepsia— the lowering of epithelial and secretory activity and capacity, of structural conditions, the consequent mal-absorption, mal-assimilation, and mal-excretion, keep up an ever intensifying circle of dyspeptic conditions, the only remedy for which,
along with carefully arranged dietary, and general habits, and environment, is the giving of rest to the digestive organs until they are restored, — by means of the regulated administration of the digestive ferments, — and even after that, it is necessary in some cases, and not a few either, for the patient’s personal medicine chest never to be without some reliable artificial digestive ready to be resorted to upon occasion.

The Preparation of Pepsin.

To obtain pepsins and pancreatin of any value, freshly procured, pure, uncontaminated, whole materials are essential. According to the British Pharmacopoeia process of preparing pepsin, a dry pure pepsin should have the following characters: — a slight yellowish-brown powder, having a faint but not disagreeable odour, and a slightly saline taste, without any indications of putrescence. This is practically a preparation of dried stomach-scrapings, and, as generally prepared, according to the bare directions of the British Pharmacopoeia, contains a variable amount of pepsin.
and becomes, sooner or later, an inert and ill-smelling substance,—the
presence being due to an excess of decomposing epithelium.

Other and evidently superior processes consist in macerating the muco-caneous
membrane of the stomach (of either a hog, calf, or sheep) in cold water for 12 hours, straining the
liquid, and precipitating the pepsin by lead acetate; the pepsin, after being washed
filtered, is evaporated to dryness at a
maximum temperature of 105°F.

Previous to evaporating, some makers
mix with starch, and, further, add
milk-sugar, or other fine sugar. Hagen
more says that unscarched pepsin
soon becomes inert and nauseous, but
these bad properties are, surely, more
likely to be due to the amount of
epithelium involved, than to the
amount mere absence of sugar, from
the presence of which, indeed, one would
rather fear fermentative deteriorations.

Such first-class firms as Bullocky,
Bonduel, Armour & Co., Parks, Davis & Co.,
claim to have devised processes whereby
a much purer and more refined dry
pepsin is now produced, the amount of
epithelium involved being reduced to an imappreciable minimum, and neither sugar nor starch is admitted. The preparations of these firms certainly keep their purity for an unlimited time, and have scarcely any odour or marked taste whatsoever. I have examined them under the microscope, with high powers, and the pancreatin by the same makers also, and found them perfectly free from starch and sugar, and remarkably free from epithelium. H. W. Kinnon has lately succeeded in dialyzing pure gastric juice, the pepsin remaining on the dialyzer. It is then dried in vacuo and pulv. urised.

The Pancreatins, and Pancreatic Extracts also, are prepared by chopping up fresh pancreas finely, and macerating in four times their own weight of alcohol and glycerine, dry pancreatin being precipitated and evaporated from these solutions by usual means.
The British Pharmacopoeia test for Pepsin requires that:

One grain of Pepsin, mixed with 2½ minims of Hydrochloric Acid, in \( \frac{1}{2} \) (one) ounce of distilled water, should digest 50 grains of hardboiled white of egg (previously passed through wire gauge of 36 meshes per linear inch, and made of No. 32 brass or copper wire), on their being well mixed, and well stirred together, at a temperature of 130°F, in 30 minutes.

The United States Pharmacopoeia test for Pepsin requires that:

One part of Saccharated Pepsin, mixed with \( \frac{7}{2} \) parts of Hydrochloric Acid, and 500 parts of water, should digest 50 parts (at least) of hardboiled egg albumen, at a temperature of 38° to 40° C, (100° to 104°F) in five or six hours.

Compared with these requirements, Asmon's pepsin professes to excel them some four times, Fairchild's pepsin some 20 times, Hühn's pepsin some 20 times, Parke, Davis & Co.'s pepsin aseptic 80 times, Schacht's pepsin liquid 20 times.
It is, obviously, an exceedingly difficult matter for a general practitioner, called away so often from the house, generally at the times most inconvenient to himself, to carry out, fully and accurately, experiments demanding his undivided attention, care, and thought. To substantiate these claims would require accurately followed experiments of 3, 4, or more hours in length, the temperature being maintained constant at about 104° F., by means of a Page's Respiration Apparatus, an apparatus somewhat difficult to get into working order. Such long-time experiments, and such substantiations, I have not attempted to carry out; but as a good pepsin is very active at 130° F., and at that temperature can achieve much in 30 minutes, I am able to state, that so far as my observations show, the above-named preparations of pepsin are certainly of exceptional activity. Especially powerful is Messrs. Parke, Davis & Co.'s "Pepsin Aseptic," the activity of which proved quite amazing. Fairchild's Pepsins have also well deserved their reputation.
The following dry Pepins are the chief ones which have come under my notice:

Armour's, Powdered (insoluble).

- Granular (soluble, non-hygroscopic).
- Bullock's Pepina Poric (an insoluble powder).
- Fairchild's Pure Pepsin (in scales).
- Parke, Davis & Co.'s Pepsin Aseptic (a very elegant scale preparation and fairly soluble).

This firm also prepare & Lamellar,

Powdered, Saccharated, Lactated Pepsin.

Savory & Moore's (Acidulated) Pepsin.

Wlath's, Pure Pepsin, of their very pretty and soluble Granular Pepsin.

Inglivin (Warner & Co.; Newberry & Co.).

All these I found to retain their purity of character after some months of keeping, and, with the exception of Inglivin, they all answered to the B.P. test admirably.

Inglivin is said to have been used long ago by the Chinese, in various ways, as a remedy for dyspepsia, chronic and acute. They prescribed the gizzard of fowls to be cut up and mixed in their dishes. It is from the gizzard of the common fowl that Inglivin is prepared.
and it claims to be remarkably and specially efficacious in acute dyspepsia, in acute gastritis, and in the vomiting of pregnancy. Professor Robert Bartholow substantiates these claims in his recent work on Therapeutics. It is said to be pancreatic in its action, as in the gizzard of the fowl it appears to act upon both proteid and starchy foods; and it can act in the presence of alkalies as well as in acids. It is announced to be given in the same dose as peptic, but such dose acted disappointingly slowly in my experiments, so slowly that I am not even able to say that Inflavin came up to the required standard of peptic activity.

Of the dry Peptins, the Granular or Lamellar preparations keep best and act best, as a rule. They are more soluble also, which is an advantage. In my experiments, Peptic Aseptic 1/2 gr. (a preparation said to render gentle aseptic by a special process) dissolved completely, 50 grains of boiled-egg albumen, according to the British Pharmacopeia Test, in ten minutes.
The same success attended exactly similar tests with Fairchild’s peptic and Aronson’s granular peptic— all granular preparations, and with Bullock’s “pepsina posci” and Wythe’s “pure peptic,” which are both exceptionally good dry powdered preparations. There was complete solution of the albumen (excluding, of course, small residues of fibrous matter, or perhaps a very slight residue of albumen), in this short time, at a 130° temperature, and in other experiments larger quantities of albumen were dissolved in times varying from a quarter to one hour. Such may be considered preparations of all the activity and trustworthiness to be expected and desired.

In all my experiments, whether with solid or with liquid preparations, I did not rely entirely upon mere solution of albumen (or of fibrin), as a test, nor upon nitric acid, or other tests for albumen, but whenever solution was going on I tested the process of the action of the peptic by means of the usual tests for peptone, along with comparison tests for albumen.
Chief amongst the tests for Peptones is the "biuret" reaction, which is carried out as follows:— Neutralize a portion of the contents of the beaker with Liquor Potassae, then add a drop of Schling's Solution (test for Glucose, the usual solution)— If peptone be present, even in small quantity, the result is a delicate rose-pink color, which is deeper in tone according to the amount of peptone present. After a little experience, one becomes familiar with the various degrees of pink obtained by different amounts of peptones, and one can therefore approximately estimate, in ready fashion, the degree of activity of the pepsin used.

Other tests for Peptones are given in the physiological manuals:—

Peptones are not precipitated by boiling Nitric Acid, or other mineral acids, nor by Acetic acid, Weak Alcohol, the majority of metallic salts, Potassium Ferrocyanide; they are not readily coagulable by heat. They are precipitated from neutral or slightly acid solutions by Mercuric Perchloride, Silver Nitrate, Lead Acetate,
Potassic—mercuric iodide, Tannic acid, Picric Acid (yellow precipitate) Bile acids, strong alcohol. Cold Nitric Acid is said to precipitate Hemalbuminose, parapeptone, or peptone, but heat does not coagulate it, and it gives the Binnet reaction like peptone.

Many of the preparations of peptic vary, largely according to the way by which they have been obtained and prepared, in the length of time required to effect solution of a constant quantity of egg-albumen (boiled); however finely divided it may be, egg-albumen swells up considerably in dilute acid conditions—in acidulated water—and therefore, peptic solution of it is often obscured until nearly the end of the experiment. It is obviously unfair, then, to judge of the action of a peptic within a given limited time, by the mere appearances, or by weight of the remaining egg-albumen, and hence the importance, especially in limited-time experiments, such as mine were, of employing the peptone tests to detect whether peptic action is really going on at all, or not. More than once
I found quite pronounced peptic action
to be going on, but from the above causes,
deceptively slow. There is another point
which one has to be very careful about
and which one observer, Professor Wisan
I believe, commented upon, viz. that
marked variations of temperature during
an experiment, retard the progress of
the digestive process, sometimes considerably,
a diminution to 85°F, or an elevation
to 150°F, I have found several times
to be almost, if not quite, fatal
to the remainder of the digestive process.

Of the Peptic Salts, — Savory
Moore's "Pepic Salt" & "Pepsalin", — and
of the Peptic Salves — Blanchard's, Savory,
and others, — I have tested only the
well-advertised "Pepsalin" (Stem & Co's)
and it responded to the test very well.
It claims to be a peptic condiment
only, to be used in the same manner
as table salt and as freely. It is very
stable, pleasant to the taste, and, as
I can testify from clinical experience,
(somewhat of a personal one), it acts promptly.
It contains a "physiological proportion
of hydrochloric acid," and is certainly
an excellent handy aid to digestion, having the advantage for some people of being in non-medicinal form. It has excellent testimonials from the medical journals from physicians of "Peppifer" (T. Howard Lloyd & Co's), I fear I cannot say much to recommend it. It claims to be a mixture of Reduced Iron, Pepsine, and freshly ground Pepper, "made up from the prescription of Dr. Sessions Barrett." Its action on albumen is, experimentally tested, very slow, if any, and is greatly obscured by its muddy mixture with water.

Of the Peptic Sauces, I can only say that the value of the pepsine by the same Makers justifies one in expecting the Sauces to be useful.

Nearly all the Leading Makers produce Tablets, Tallowds, and Pills, of pepsin; several of these I have tried, clinically, and experimentally, and I believe they are genuine; their portability is the peculiar value of their form, and it supplies a need, for travellers & Commercial people.
The following is a list of the chief preparations, as advertised:

- Armant's Pure Pepin Tablets.
- Bullock's Pepin Pills.
  " " " Lactose.
  " " " Cam Charcoal.
  " " " Capsules.
- Burgers' Pepin Pills.
- Allen & Hanbury's Pepin Tablets.
  " " " Papain.
- Fairchild's Pepin Tablets (aromatic and acidulated).
- Parks, Davis & Co's Pepin Lactated Tablets.
  " " " Pepin and Bismuth.
  " " " Pure Pepin (1/4) Pills.
  " " " Argemaraned Digestive Tablets.
- Savory & Moore's Pepin Lactoses.

Speaking of the Liquid Preparation of Pepin suggests the question, what are the best fluid preservatives of the digestive ferments? Bromic acid solution makes large doses of pepin intolerable. A 12 to 15 per cent extract in rectified Spirit does better, and the alcohol is easily driven off by simple cold or heated evaporation, — if objected to. The same may be said for Chloroform.
Amongst such liquid—water and alcoholic—preparations are the numerous Pepsine Wines, Elixirs, Cordials, and Essences. Some of these non-alcoholic "liquors" of Pepsin are probably simple solutions of granular, soluble, dry pepsins, such as the numerous liquors Pepsin—Bismuth. Many of these "liquors" are made still more valuable, clinically, by their combination with acknowledged cholagogue tonics.

Such are:

Oppenheimer's Diger Eurymin et Pepsine C.
" " " " ~ Pepsin et Bismuth.
" " " " ~ et Cassara.
" " " " ~ et Podophyllin.
" " " ~ et Palatella.
" ~ Alkaline et Pepsine C.

Mead's Peptic Essence ~ Eurymin
" " " ~ Bismuth C.

Rockin, Wilson & Co's Dig Pepsin et Podophyllin.
Schacht's Dig Pepsin ~ Eurymin ~ Bismuth C.
" " " ~ Eurymin.

Representatives of these, I have tested carefully, and found that their digestive capacities were such as to make them distinctly useful preparations, whilst clinically their cholagogue made them still
more useful. The above-named may
well be considered valuable preparations.
Stoeckis, Guder, & Armont's preparations
of peptic wine, have proved most
valuable in cases of anaemia, with
atonic dyspepsia. Experimentally, their
digestive capacities are not so easy to
follow; they require some hours to
complete solution of albumen, and
intermediate stages are somewhat
obscured by the presence of the iron.
The trustworthiness of the pepins by
the same makers, — of all these compound
preparations, — is very assuring, however.

The following is a list of the simple
liquid extracts and solutions, of
pepin, by the principal makers:

Schacht's Pepinia liquida.

(may be combined with dimethy)

Bulkhead's peptic wine.

Savory & Moore's Vinum Pepticum

Howard Lloyd's Peptovine

Metcalfe's Vinum pepinum

Aidos-

Parker, Davis & Co's pepin cordial

""""Pepina Liquida (U. S. P.)

"""""Pepine Lime Juice.

Oppenheimer's Lig Pepina Acidum.
Shackto, Repasa Sieruida is a beautiful, aseptic, simple fluid preparation, keeps splendidly, and is of such pleasant taste that it can be taken along with a meal, even by children. Its makers, (Messrs. Jules Shackto & Co.) claim that one fluid drachm of it can dissolve 1000 grains of egg-albumen. I have not attempted an experiment so long as to be able to prove this claim, but I can testify to its digestive powers being of a very high order.

So also of Pepsim Cordial, (Parke, Davis & Co.), a very elegant and palatable, alcoholic, carminative preparation.

Glycerine is, however, the most powerful absorbent and preservative of the digestive ferments, and no preparations (liquid) give such uniformly satisfactory results, in test experiments, as the glyceroles and acid glycerines of pepsim prominent amongst those advertised are:

Horner's Acid Glycerine of Pepsim.
Armour's Essence of Pepsine (?).
Beedale's Peptic Essence.
Benzer's Liquor Pepsins.
Savory & Moore's Succus Pepsins.
Armon's Glycerole of Pepsine (10 minims contains one grain of Pepsine)
Bullock's Acid Glycerine of Pepsine, which has long had a well-deserved reputation.
Parke, Davis & Co.'s Concentrated Glycerole of Pepsin (Same strength as Armour's)
Savory & Moore's Pepsine Elixir, which is an acid glycerine.
Fairchild's Glycerinum Pepsicum (5 grains of pepsin to one drachm of glycerole).

All these are elegant and palatable preparations, and retained their purity of smell, taste, and appearance after six months keeping in a cool dark cupboard; Lorimer's was the only one that deposited a little. They are all compatible with any desirable additions which can be mixed with glycerine & with acid. I have examined Lorimer's, Armour's, Beedale's, Benzer's, Savory's, & Fairchild's, in particular, with the following results:
They are all prescribed in doses of one to two drachms. In my short experiments, 50 grains of egg albumen (finely divided, after being boiled ten minutes) in half-an-ounce of water, acidulated with 25 minims of Acid Hydrochloric dil. (B.P.), at 130° F., were completely dissolved by:

- Lohr's Glycerol, 20 minims, in 30 minutes.
- Fairchild's " 20 minims, in 20 ".
- Ringer's Lys. Phosphate, 20 " 30 ".
- Armon's Glycerol, 30 " 30 ".
- B. d'Aubert's, 30 " 60 ".

(this was very tardy, compared to its claims).

Savory's acted rapidly upon cold roast-mutton-fibre, upon shreds of which I obtained steady action with all the other pepsin preparations commented in this Thesis.

These short-time experiments, in their above-mentioned results, testify, in all requisite fulness to the digestive capacities, continued through longer more natural periods of time, of these and of the following preparations:
Summary of other experiments with preparations of pepsin, each tested under same conditions, viz., 50 grains of finely-divided, boiled egg-albumen, in ½ oz. of water (acidulated with 25 minims of hydrochloric acid) at constant temperature of 130°F.:

<table>
<thead>
<tr>
<th>Preparations</th>
<th>Quantity Used</th>
<th>Complete Solution in</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bullock's pepsina porci</td>
<td>½ gr.</td>
<td>25 minutes</td>
<td></td>
</tr>
<tr>
<td>Fairchild's scale pepsin</td>
<td>½ gr.</td>
<td>20 dc.</td>
<td></td>
</tr>
<tr>
<td>Wyeth's pure pepsin</td>
<td>½ gr.</td>
<td>20 dc.</td>
<td></td>
</tr>
<tr>
<td>Pepsin Asepto</td>
<td>½ gr.</td>
<td>0-15 dc.</td>
<td></td>
</tr>
<tr>
<td>Pepsin Cordial</td>
<td>3.55</td>
<td>30 dc.</td>
<td></td>
</tr>
<tr>
<td>Wyeth's Chjir</td>
<td>3.55</td>
<td>30 dc.</td>
<td></td>
</tr>
</tbody>
</table>

(of which, more hereafter)

Pepsalia 20 gr. 30 dc.

Papain, or "vegetable pepsin," is an artificial digestive which has given rise to special interest, and its value and capacities have been much discussed, although there is not much literature about it. It is now generally
acknowledged to be of considerable value, clinically, and I find many fellow-practitioners constantly and largely using it with considerable satisfaction, whilst to others its virtues are doubted or but little known. Papain is obtained from the juice of the fruit and of other parts of the Papaw, or melon tree, Carica papaya, its vegetable origin being of itself no small recommendation to some people. Its peculiar properties are agreed upon, or as stated, by such special observers as Pinker, Herschel, and Sydney Martin, are as follows: Its solvents action upon proteids, such as albumen and fibrin, resembles that of pepsin, that upon milk resembles the action of trypsin, but is much less rapid, and therefore its peptonizing action can be the more readily arrested at any intermediate stage. It will curdle milk under exactly the same conditions as the gastric rennin. One of its great differences, in action, from pepsin, is that it cannot digest proteids in acid, except the acid be less than one-fourth the strength of the gastric hydrochloric acid. It can act equally
well in neutral or alkaline solutions, and it acts best in solutions which are concentrated. Since Papain may claim to be our best digestive aid in cases of dyspepsia where a large ingestion of fluids is undesirable, (Several ounces of water appear to be necessary in all peptic digestion), as in dilatation of the stomach, and in some cases of chronic atomic dyspepsia. Here too, is a digestive remedy, or aid, which can be combined with alkales.

Upon these important points it has been cordially recommended by the medical journals, and by leading physicians, and my own humble clinical experiences can testify to the value of papain in dyspeptic conditions, even of a severe and troublesome character. Seymour Hamilton's Liquid Papain, Walker & Co., was the first preparation of papain which came under my notice, and I have used it extensively. I am able to say, that whenever I have used it with careful appropriateness, I have never found it to fail in giving speedy and lasting relief, and in restoring the digestive organs to normal activity.
more especially in cases of acute or chronic dyspepsia where there has been persistent epigastric pain coming on very soon after meals, with pain about the shoulder-blades, repeated vomiting, or troublesome exertions of sour and fetid gas and food, where there was need for so excellent a hepatic stimulant as Iridin. But these cases improved too rapidly, and from conditions too established and prolonged, to be put right by the Iridin alone. The papain I have found, from careful observation, was of real and essential value, as well as the Iridin. This preparation (e.g. Papain at Lloyd Co) is slightly acid, and is best prescribed alone, unless with carminatives. One case, from amongst many others which I have treated with this, and with Lloyd's and Tindeo's preparations, I had some few years ago, gave strong testimony, in its result, to the value of papain. A man, A.E., aged 35, of good family history, and with a family good personal history, had suffered for some days from severe epigastric pain, persistent vomiting of all ingesta, alternating...
diarrhea and constipation, rapid loss of flesh and strength. There was no discoverable cause, no discoverable swelling, but notwithstanding that, and the absence of biliary vomiting and of hematemesis, the acute persistence of the symptoms, and the utter failure of all ordinary stomachic sedatives, and of external counter-irritants, tended to an increasing fear that there was malignant disease as the cause. At last I tried a sample I had of Seymour's Dig. Papain. The result was quite amazing. Within a few hours all the above-named symptoms disappeared, and the patient speedily regained full health and flesh. Two years afterwards I met him actively engaged in the pursuit of business, and in good health. Apparently the case was one of remarkably severe "acute gastritis," and very prolonged.

Another patient, a man, aged 50, suffers now and again, from acute gastric catarrhal attacks, due apparently to the inhalation and accidental swallowing of sweet particles floating in
the air, and covering everything, in his workshop, a "sweet" factory. Nothing has ever afforded him such speedy relief as papain, and he resorts to it at once when attacks come on.

Papain is not destroyed by quinine, nor by antiseptic acids, nor is pepsin - it is said to have remarkable solvent powers upon diphtheritic and croupous membranes, and it also dissolves the unhealthy mucus of gastric catarrh, (as shown, I believe, in my case, A.E.), of fermentative dyspepsia, of dilatation of the stomach - I have not had an opportunity of testing its solvent powers upon diphtheritic membrane.

It is my opinion, judging from experimental observation, that papain acts best in neutral, or almost neutral, conditions.

Dr. Finkler's Papain (agent, B. Kuhn, London) claims to be capable of dissolving 10,000 times its weight of albumen or fibrin - I have not attempted an experiment long enough to prove this claim, but my experiments gave most
satisfactory results in the digestion of albumen, of fibrin, and of casein—so also with Lecorns and Lloyd's Papains. I cannot say, however, that they excel the best papains in digesting power, indeed they are markedly slower. At one time I fancied that papain digested starch, but further careful experiments proved that papain had not that power at all. Finkler's papain is a powder and contains both starch and sugar, as vehicles I suppose. It will keep in water only a few days, but a few grains of hydrochloric acid acts as a sure preservative; hence its presence in the liqueurs' papain Co.

The powdered papain is prescribed in one or two grains taken before or after meals. There are pearl-coated pills, (1 gr. or 2 gr. of papain in each), and lozenges (same doses), and Tablets (2 gr. of papain + 2 gr. Soda Bicarb., to be taken before meals). There are also liqueurs with Acid; Hyoscine, with Bismuth, with Indin, with Cascara Sagrada, 7½ grains of dry papain will peptone one pint of milk and water in ½ hour, sufficiently for digestion. Toward Lloyd & Co. Liqueur Papain Co., contains Eumirin & Nuton.
There are several Compound digestive preparations, containing peptic, pancreatic, and either Diastase, or ptyalin, and, in some cases, either hydrochloric or lactic acids, or both, — about which there is much theoretical and clinical dispute. These are:—

John Morgan Richard's Lactopeptine, Hayen Morosé's Maltopepsyn, Parke, Davis & Co's lactated peptic, Myeltho 'Elixir of the Digestive Ferments.' About Allen and Henbury's hypo-pepsin, Hypo-Pancreatin, & the Kepler Malt Extract with Pepsin & Pancreatin, there can be no dispute; they are preparations which at once prove their worth, my experiments with them meeting with beautiful and rapid results.

**Lactopeptine consists of:**

- Pepsin 8 parts
- Pancreatin 6 parts
- Diastase or ptyalin, 4 parts
- Lactic Acid, 2
- Hydrochloric acid, each 5¼
- Milk Sugar 40 parts

**Maltopepsyn (or Dyspepsyn) =**

- Pepsin Sacch., one part
- Pancreatin Sacch. ½
- Acid Lactophosphate of Lime ½
- Malt Syricate 2
This preparation is much cheaper than lactopeptine. - It contains no free acid, no sugar, as the makers believe that these are the causes of the decomposition of dried peptone preparations.

Lactated-Pepsin (Parke, Davis & Co.)

Pepsin, Pancreatin, Diastase, Maltose, Hydrochloric and Lactic acids; proportions not published.

Dry.

All these preparations are very palatable, odorless, and miscible, and they all appear to retain their purity after long keeping. But they are, in my belief, all surpassed, theoretically, and in experimental evidence, by Wyeth's "Elixir" which is a glycerine extract of pepsin (hog's and calf's), rennin, and amylopsin. It is a preparation of great purity and activity, and I can go far in substantiating its high claims; 20 minims of it dissolved 50 grains of finely divided, boiled egg-albumen in acidulated water, in 20 minutes. It contains no acids whatever, but it can
curdle milk in large quantities. It is exceedingly palatable and elegant, and digests starches as rapidly as it digests proteids. Clinically also, I have found it an admirable preparation - Fairchild's Peptonic Tabloids.

I have found very useful in several cases of chronic dyspepsia. They consist of an inner kernel of Glycine (Pancreatin) with calcium lactophosphate, enclosed in a coating of keratin, and an outer shell of pepsin enclosed in an intermont coating of fine sugar. The inner kernel of Glycine is supposed to survive the pepsin shell until it reaches the duodenum, beyond the ravages of hydrochloric acid.

These dry preparations all seem admirably designed and clinically attractive, and they are well-prepared. In many cases of chronic dyspepsia, or of temporarily enfeebled digestive powers, as during, or after some febrile attack, it is logical to conclude that the pancreatic secretion is probably as feebler as the gastric secretion,
that there is as much need for the administration of ptyalin and pancreatin as for that of pepsin. These compound preparations should hence supply a real need. Professor Attfield considered lactopeptin to be of much superior power to pepsin alone. The dry preparations all make this claim, which is surely not excessive, of course, seeing that in them trypsin is superadded to the pepsin, whilst on the other hand many pepsins (by inferior makers) are but of indifferent quality. These dry compounds have all received considerable clinical testimony, and my own experiences value lactopeptin and Maltopepsin highly. The former, especially, has been of immense service in cases, not only of dyspepsia of a catarrhal character, but also in cases of anemia, infantile diarrhea, gastric ulcer, neurotic conditions. Indeed, these compound preparations are more prescribed nowadays, I believe, than the simple dry or liquid pepsins and pancreatin.

But mine are not the only experiments with these preparations, that are somewhat
perplexingly disappointing, and they bring up questions about which much contradictory opinion has been expressed by various observers, viz.: Are pancreatic and phytalin (or Diastase) compatible with hydrochloric acid? Are they destroyed or in any way affected by that acid, or by lactic acid?

Defresne's experiments led him to assert that these two ferments can both resist the gastric acids during their stay in the stomach, although certainly hindered in their activity. But, that after passing into the duodenum, they resume their activity at once, upon meeting with the alkali of the duodenal secretions.

Sir Wm. Roberts (in the Lumholt lectures before referred to), claims to have disproved these experiments of Defresne's. He says that lactic acid is nearly always present, if ever, not essential to normal digestion. (The general understanding is that lactic acid is only a by-product of starch digestion and that, in excess, it is one of the commonest causes of...
"heartburn" and sour conclusions). Sir Wm. heated a proportionate mixture of pepsin and pancreatin, at 100° F., with a 0.1 per cent lactic acid solution, for one hour; and then added some egg-albumen. After a due interval, he tested and found, he says, that the albumen "was entirely unaffected." He therefore concluded that the ferment had been destroyed altogether. With all due respect to so eminent a teacher as Sir Wm. Roberts, I am convinced that there are several fallacies in his experiments:— (1) Why not have used hydrochloric acid, the proven, constant, normal acid of gastric digestion, the very acid at stake? (2) If lactic acid be a normal essential in gastric digestion, as Sir Wm. Roberts asserts, then why did not the lactic acid and pepsin digest some of the albumen, even presuming the pancreatin to be paralyzed by the acid? Pancreatin cannot destroy pepsin— (3) If lactic acid is only a by-product of digestion, as is most generally believed, then is it not possible that even so small a percentage as 0.1 per cent was more antagonistic
to the pancreatin and to the pepsin, than it could be helpful. There is no reason to suppose that lactie acid could favour the action of either pepsin or pancreatin.

(4) It would have been more exact, from a physiological point of view, to have allowed the ferments to act upon the albumen from the very first. As it was, there does not appear to me to be any justification for the heating together of the pepsin and pancreatin with lactie acid, for so long before subjecting albumen, or other digestible substance, to their action; with nothing for them to digest but each other: indeed, with lactie acid, some fatality may have happened to one or both of them in Sir W's experiments. Pepsin and pancreatin, with either lactie or hydrochline acids, are certainly not stowing together in the stomach for one hour preparatory to the ingestion of food. Sir W had an excellent accidental opportunity of discovering, that in a perfectly healthy person, the contents of the stomach were markedly acid, even three hours after the ingestion of an ordinary meal. To portions of these acid ingesta he added pancreatin & saliva,
but found that after one hour's digestion at 100°F, they had no further effect upon either starch or milk. He again concluded that the ferments were altogether destroyed, not neutralizing the acids, and then testing the action of pancreatic and saliva in normal condition, when he would probably have found that their action had been only temporarily suspended.

I have carried out a series of experiments relative to this matter, but have dealt only with hydrochloric acid, the general opinion of present-day physiology justifying the exclusion of lactic acid altogether. My results and conclusions may be briefly stated as follows:

1. An excess of hydrochloric acid with saliva and arrowroot (boiled) resulted in no change, even after neutralization of the acid. The excess acid appeared therefore to destroy the phlegalin.

2. But very slight acidity (less than one-fourth the gastric-juice proportion) did not prevent the formation of achoo-dextrins, & even of maltose, from arrowroot. The phlegalin was acting.
though only partially.

3. Hydrochloric acid, in rather less than the gastric-juice proportion, did not destroy the action of pancreatic upon starch. I obtained an excellent, though delayed, reaction of sugar and aehrodextrins, which was more abundant after I had neutralized the acid. These constituents of the experiment were put together at one and the same time, and heated up to 100° F., along with arrowroot starch. The acid and the pancreatic were not "stirring" together for one hour before the starch was added.

4. The presence of Pepsin made no difference to the results of Experiment 3.

5. Pepsin, without hydrochloric acid, did not prevent the action of trypsin upon albumen.

6. And finally, a digestion of albumen and starch mixed, by pepsin, pancreatic, and a slight trace of hydrochloric acid, resulted in marked success, after one hour's digestion, with both the albumen and the starch. The pancreatic and pepsin used were non-saccharated.
My experiments coincide, therefore, with the experiments of Mr. Arnold Lee, and with the teaching, as I believe I correctly remember it, of Professor Rutherford (1886): viz., that pepsin can act in a small proportion of hydrochloric acid, but that full gastric proportion appears to arrest its action, at least, possibly to destroy it; that pancreatin can act in a considerable proportion of hydrochloric acid, which, if it does arrest the action of pancreatin, does so only temporarily, pancreatic action being resumed after neutralisation of the acid, or upon diminution thereof.

There is therefore some considerable experimental corroboration of the general clinical estimate of lactopeptine and allied compound preparations. The action of these dry compounds is, as I have before stated, disappointingly slow in experiments upon albumen. Dowdwell, Jason, and other observers noticed the same thing — is this due to any intrinsic change in the complex composition of these dry compounds, which may take place during keeping? No such changes are apparent in their general appearance.
Or is the disappointment due to the fact, that, even in the most carefully designed experiments, we cannot possibly imitate all the exact conditions and changes, chemical and physiological, of so complex a process as that of natural digestion; and that, therefore, some selective influence is at work regarding the action of these compounds, in the living stomach, (making them of real value as clinical experiences seem to prove), which we cannot possibly have at work in experiments outside performed outside the stomach of living organisms? But, although solution of Albumen by Lactopeptine & Maltopeptin apparently takes some hours to complete, at an early stage, (within the first hour), the peptone tests revealed peptonization to be going on (in my experiments), and the glucose + iodine tests, compared, revealed the steady progress of starch digestion.
The following are the chief preparations as advertised of the Pancreatic Enzymes:

**Powdered:**

- Armour's Powdered Pancreatin.
- Allen & Hanbury's Extractum Pancreaticum (Saccharated)
- Parke, Davis & Co's Pure Pancreatin.
- " " " Saccharated C.
- Savory & Moore's Powdered Pancreatin (made also in Rolls & Franks)
- Fairchild's Trypsine (non-saccharated).

"Reptonizing Powders":

- Allen & Hanbury's (Consist of Std. Panco, with Soda Bicarbonate)
- Berger's (Pulv. Pancreaticus Alkalins, contain Pancreatin & Soda Bicarb)
- Fairchild's (5 grains of Pancreatin, with 15 grains of Soda Bicarb, usefully enclosed in glass tubes)

**Reptonizing Tablets:**

- Armour's Pancreatin & Soda (2 1/2 gr) (8 gr)
  - Parke, Davis & Co's (Separate Tablets of Soda Bicarb, 10 grains; Separate Tablets of Pure Pancreatin, 2 1/3 gr)

- Savory & Moore's Pellets (Require little alkali, quick in action, weigh 5 grs.
- Fairchild's Trypsine Tablets (3 gr; 20 Soda)
Glycerols and other liquid preparations:

- Armouso (from which a peptonising "liquor" is prepared by the addition of soda bicarbonate).
- Bleachadale Pancreatic Essence (fleshy)
- Berger's Liqueur Pancreatic.
- Allen and Burnby's Bovine Pancreatin (mallaled pancreata.
- Baske, Davis, & Co. liquid Pancreatin.
- Savory & Moss's Succus Pancreatic.
  (a glycerole, or "essence", for dosage, or for peptonising)
- Savory & Moss's Saline Essence Pancreatin.
  (an agreeable ketchup or sauce)
  (for the administration of cod-liver oil)
- Kepler Malt Extract- with- Pancreatin.

If pancreatin be administered, in medicinal doses, apart from food, it is certainly better to give it before a meal. Better still is it to mix proper proportions with the food, without alkali, at 100°F, about 20 minutes before taking the food, which should then be taken slowly, as Sir Wm. Roberts has taught. Best of all is to predigest, or "peptonise" the food with a pancreatin & soda, before it be taken.
I have performed digestive experiments with most of these pancreatic preparations, upon albumen (egg), cooked meat, arrowroot starch, milk, with results as follows:

Armour's preparations are fairly active, but don't keep very well, and have rather too much of a meat-extract smell and taste.

Allen and Hanbury's, Savory & Moore's preparations are all that could be desired.

Fairchild's, and Benger's, fully supported their reputation, and were rapid in operation. Peptonised milk prepared with them is of excellent flavour.

Beecham's tincture was very disappointing.

*(Those marked X were experimentally tested)*

On the whole, it is remarkable that the pancreatic preparations seem to be of equal quality and capacities. There is far less room for doubt about them than about the pepsins, but this is no doubt due largely to the fact that such fabulous claims have been made regarding many of the pepsins, which are difficult to support.
And further, so many of the dry peptones were probably prepared, formerly, by methods, resulting in preparations which have become inert and nauseous. The liquid preparations of both peptic and pancreatic "have always been superior," and still hold their position as to purity, quality, and reliability, (i.e. those by aforesaid manufacturers), but improved methods have produced dry peptones of equal purity and quality and capacity to the liquid ones.

Peptonising foods — milk, gelatine, jellies, blanc-manges, soups, beef-tea, &c — is best done in the kitchen. As required, this is much the cheaper and easier way also. All the peptonising powders, tablets, &c, perform their duties in much the same conditions, and their accompanying "directions for use" are easy to follow, in every case. It is superfluous to speak of the clinical value of peptonised foods, prepared at home — but the following foods, prepared ready to use this. I have
met with and may comment upon, in concluding what I humbly claim to be a serviceable thesis, and a helpful contribution to the therapeutical literature of the day.

**Special Peptonised Foods (advertised and tested):**

Armour's "Nutrient Wine of Beef-peptone" does contain true peptones, but my specimen became offensive at a very early date.

Mozzera's Beef-Meal, *T* Beef Cacao, are beautiful and useful preparations.

Carnick's Beef-Peptonoids are rich in true peptones & form an elegant and, clinically, most valuable preparation. A convalescent case of typhoid delighted in it, as also in Horlick's Malted Milk, which I cannot commend too highly, from further observation also—

Savory & Moore's peptonised Milk, *T* peptonised Cocoa & Milk, are also worthy of the highest commendation.
so also their "Meat-peptone".

Bengar's Peptonised Beef-Jelly, and
Chick'n-Jelly, & their famous
"Food" for infants & children, are
truly worthy of their reputation.

Hemmorich's Peptone of Beef satisfies
all requirements.

Pinkler's Papain-pepton (Kuhl) is
a very concentrated, miscible,
and carefully prepared peptone,
papain being its peptonising
origin. It is described as containing
66 per cent of peptones. Though
dry it is very stable. It is very
readily dissolved, and is altogether
a highly interesting & useful
preparation. So also I believe
are Papain-pepton, Cocoa and
Papain-pepton-Chocolate.

Savory & Moore's, & Fairchild's,
Peptone Suppositories are elegant,
non-offensive in general character;
they keep well, and contain good,
true peptones, evidently in large quantity.

Signed: Edmund H. Smith, M.D., F.C.S.