COMPARISON OF THE PHARMACOPŒIAL METHODS FOR THE DIGESTIVE FERMENTS AND ANIMAL PRODUCTS ADOPTED BY THE DIFFERENT COUNTRIES.*

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In January, 1817, Dr. Lyman Spalding of New York City, submitted to the Medical Society of the County of New York, a project for the formation of a National Pharmacopœia, and on December 15, 1820, the first issue of this national volume was published in Boston, in both Latin and English. There have been eight revisions since this first volume appeared, and the present book stands pre-eminent as a national standard, having been adopted by the United States Department of Agriculture.

Section 7 of the Food and Drugs Act of June 30, 1906, states: "In the case of drugs, if where a drug is sold under or by a name recognized in the United States Pharmacopœia or National Formulary, it differs from the standard of strength, quality or purity, as determined by the test laid down in the United States Pharmacopœia or National Formulary, official at the time of investigation, it is deemed to be adulterated unless said difference is plainly stated on the label." Nor is the United States alone in its publication of such an official standard; indeed, each nation has its own standard volume. In France they have the French Codex, in Germany the Arzneibuch, in Japan the Japanese Pharmacopœia, and in England and her colonies the British Pharmacopœia, etc.

I shall not attempt a general comparison of these various books, but will confine myself to the requirements of the various governments for the standardization of the digestive ferments and animal products.

The digestive ferments which have received almost universal recognition are pepsin, pancreatin and diastase, and of the allied animal products desiccated thyroid glands, oxgall, both pilular and purified, and peptone have been recognized.

PEPSIN.

Taking up the consideration of the enzyme pepsin, it is found that three nations, namely, the United States, Germany and Japan, evaluate the proteolytic value of this ferment by its digestion on boiled egg albumen; the country utilizing a different proteid being France, which has adopted as a proteid, washed fibrin from pig's blood, strained by hand and desiccated at 40° C., either in a warm closet or in a draught of warm air, then pulverized.

The official strengths vary from 1:400 to 1:3000, and the time of digestion from two to six hours.

The following chart illustrates the essential details of the various tests:

* Read before the Detroit Section of the American Chemical Society.

Country	Pepsin gm.	PROTEID: Egg Albumen: Boiled	PROTEID: Egg Albumen: Amount	PROTEID: Egg Albumen: Texture	Des. Fibrin Amount	Media for Digestion	Time Digested	Temperature	Official Strength	When	Kind Official	Animal Used
U. S. A.	.00333+ gm.	15 min.	10 gms.	Through No. 40 sieve		40 cc. .3% HCl	2½ hours	52° C.	1:3000	Insoluble residue after standing ½ hour does not measure more than 1 cc.	Scale, Grain or Powder	Pig
An Essence of Pepsin N. F., each fluid drachm of which contains 1 grain of 1:3800 Pepsin												
England	.005 gm.	15 min.	12.5 gms.	12 meshes to cm. No. 4		125 cc. .2% HCl	6 hours	40½° C.	1:2500	Only a few small flakes remaining	Grains, Scales, Powder	Pig, sheep or calf
Glycerin of Pepsin, each fluid drachm of which contains 5 grams of official Pepsin												
Germany	0.1 gm. Mixture made by mixing 65 parts by weight of Pepsin and 935 parts by weight of Sugar, pure	10 min.	10 gms.	No. 60 sieve		100.5 cc. .2% HCl	1 hour	45° C.	1:4000 (U. S. P.) 1:1535	Albumen must have dissolved	Saccharated	
Japan	0.1 gm.	About 6 min.	10 gms.	No. 4		100.5 cc. .15% HCl	2 hours	45° C.	1:600 (U. S. P.) 1:100 (J. P.)	Albumen almost completely digested. Moisture not over .5%. Ash not over .5%	Saccharated only	Hog or cattle
France	0.1 gm.			Pulverized	2½ gm. Desiccated pig Fibrin	60 grams .256% HCl	6 hours	50° C.	1:3000 (U. S. P.) 1:600 France	10 cc. of the cold and filtered digested solution should not at the ordinary temperature become cloudy by the addition of 20 drops of HNO_3 (sp. grv. 1.394 @ 15° C.)	Thick paste, powder or scales Amylaceous and Lactated Pepsin	

As to the general physical characters, they all agree that the pepsin should be soluble in water and also alcohol of 20 to 30 percent strength and insoluble in strong alcohol.

PANCREATIN.

Pancreatin, the second enzyme to be considered, is as the name implies, a mixture of the enzymes naturally existing in the pancreas of warm-blooded animals and consisting principally of amylopsin, trypsin, steapsin and myopsin. Of this mixture amylopsin, or the starch digester, and trypsin, or the pancreatic proteolytic ferment, are the only two enzymes which are officially standardized; and the same difference is noted with the methods adopted for trypsin as for pepsin, namely, three of the countries under discussion have adopted cow's milk as the medium for tryptic estimation, while one, France, uses the desiccated blood fibrin from pig's blood.

The chart on the next page illustrates the official methods for determining the tryptic value of a pancreatic product.

Of the animal products recognized are oxgall and thyroid glands; with peptone official in the French Codex only:

OX GALL PURIFIED.

Country	Description	Character of Product	Odor	Taste	Official Tests and Requirements Should be
U. S. A.	Evaporated Gall of Ox	Yellowish Granular soft solid	Peculiar	Partly bitter. Partly sweet.	Completely soluble in water. Completely soluble in 94% alc. Completely soluble in 50% alc. Sulphuric acid identification test.
England	Evaporated Ox Gall	Yellowish Granular Hygroscopic substance	Peculiar	Partly sweet. Partly bitter.	Completely soluble in 90% alc. and water. Also aqueous soln. gives no precipitate upon the addition of 90% alcohol. Usual H_2SO_4 identification test.
Japan	Evaporated Ox Gall				No official purified product. A crude evaporated gall is official with an ash requirement of 8.10% solid residue.
Germany					No official product.
France					No official product.

DESICCATED THYROID GLAND.

Country	Animal	Character	% Composition	Ash	Standard Requirements
U. S. A.	Sheep	Yellowish Amorphous Powder	1 part represents approximately 5 parts of fresh gland	Not over 6%	Qualitative test for presence of organic Iodine, also absence of inorganic Iodine. (9th Revision — .17 — .23% Iodine.)
British	Sheep	Light dull brown powder. Pinkish turbid liquid	100 minims, or 6 cc., represents 1 entire gland		
Japan					No official product.
France					No official product.
Germany					No official product.

PANCREATIN—TRYPSIN ESTIMATION.

Country	Official Product	Amount Enzyme gms.	Amount $NaHCO_2$ gms.	Dissolved in	Amount Milk	Digested at	Time Digested	Requirement to be Official
U. S. A.	Powder	.28	1.5	100 cc. Tepid water	400 cc.	38° C.	30 mins.	Small portion mixed with three times its volume of water and some Nitric acid added should produce no coagulation.
England	Liquid	2 cc.	0.2 gm.	20 cc. Water	80 cc.	45° C.	1 hour	Coagulation should no longer occur upon addition of Nitric acid.
Japan	Powder	.28	1.5	100 cc. Tepid water	400 cc.	38° C.	30 mins.	Requirement same as U. S. P.
Germany								Not official.
France	Powder	0.2 gm.		60 gms. Distilled Water	2.5 gms. Desiccated Fibrin or 10 gms. dried in air.	50° C.	6 hours	Filter:—10 cc. of clear liquor should not become cloudy by the addition of 20 drops of Nitric acid. (Sp. Grv. 1.394 @ 15° C.)

PANCREATIN—ESTIMATION OF AMYLOPSIN.

Country	Amount Ferment	Official Product	Starch grams	Distilled Water	DIGESTED		Iodine Solution	End Point
					Time	Temperature		
U. S. A.	0.3 gm.	Powder	7.5 gms.	200 cc.	5 mins.	40.5° C.	2 drops N/10 I. in 60 cc. water.	Converted into substances soluble in water. Four drops of converted starch solution should give no color, or at most only a wine red when added to the Iodine solution. Under these conditions 1 part pancreatin digests 25 parts of starch.
England								Not official.
Germany								Not official.
Japan								Not official, see Diastase { Japan Pharm. { See below.
France	.05 gm.	Powder	5 gms. Potato	100 cc. Water	1 hour	55° C.		A fluid liquid is obtained which, when filtered, reduces 4 times its volume of Fehling's solution.
DIASTASE.								
Japan	.05 gm.	Powder	5 gms. Potato	100 cc. Water	2 hours	55° C.		10 cc. of digested starch solution should completely decolorize 40 cc. Fehling solution.

The last product to be considered is peptone, and this is recognized by but one nation, namely, France, under the title Peptone Medicinal.

It is official as a pancreatic or peptic digestive product of albuminoids; is almost completely soluble in water, not coagulated by heat nor by the addition of nitric acid; it has a peculiar odor and a bitter taste when made by pancreatic digestion and a bitter and saline taste when made by peptic digestion.

A perusal of the before mentioned variations in the official methods adopted for the standardization of animal products by the various countries, shows that physiological chemists in general have not as yet adopted uniform methods along this line of chemistry. I predict, however, that with the advent of the next issue of the United States Pharmacopœia our foreign neighbors will admit our superiority not only in the manufacture of this important line of pharmaceuticals, but also in their standardization, and will adopt not only our products but our methods as well.

STANDARDIZATION OF SODIUM THIOSULPHATE VOLUMETRIC SOLUTION.*

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A reference to page 563 of the U. S. P., will show that the official method of standardizing sodium thiosulphate V. S., is to employ a decinormal solution of potassium dichromate proceeding as follows:

"To a solution of about 1 gm. of potassium iodide (Potassii Iodidum, U. S. P.), in 10 cc. of diluted sulphuric acid contained in a flask of about 500 cc. capacity, add slowly, from a burette, 20 cc. of tenth-normal potassium dichromate V. S., shaking after each addition. Place a watch-glass on the mouth of the flask and allow it to stand for five minutes, then dilute the solution with about 250 cc. of distilled water, add some starch T. S., and then, from a burette, the trial solution of sodium thiosulphate, in small portions at a time, shaking after each addition, and, toward the end of the operation, reducing the flow to drops, until the blue color of the mixture changes to a light green; note the number of cc. of the trial sodium thiosulphate solution consumed. Then dilute the sodium thiosulphate solution so that equal volumes of it and the tenth-normal potassium dichromate V. S. will exactly correspond to each other under the above conditions, at 25 deg. C. (77 deg. F.)."

On page 549 of the U. S. P., volumetric iodine solution is directed to be made by the following:

Tenth-normal iodine V. S. may be prepared according to either of the following methods:

"1. Dissolve 12.59 gm. of pure iodine (see below) in a solution of 18 gm. of potassium iodide in 300 cc. of water. Then add sufficient water to make the solution measure, at 25 deg. C. (77 deg. F.), exactly 1000 cc. Unless freshly prepared, its strength should always be determined anew at the time it is used. Transfer the solution to glass-stoppered vials.

Preparation of Pure Iodine.—Heat powdered iodine (Iodum, U. S. P.), in a porcelain dish placed over a bath of boiling water for twenty minutes, and stir it constantly with a glass rod, so that adhering moisture, cyanogen iodide, and most of the iodine bromide and iodine chloride, if present, may be vaporized. Then transfer the iodine to a porcelain or other non-metallic mortar, and triturate it with about 5 percent of its weight of dry potassium iodide, so as to decompose any remaining iodine bromide and iodine chloride. Then return the mass to the dish, cover it with a glass funnel, and heat the dish carefully on a sand-bath. Detach the

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