cotton an excellent deodorant for the foul odor present in pemphigus vegetans. A powder made of equal parts of talc and sulicylic acid may also be used.

In looking over the literature of the drugs and applications used in pemphigus, one cannot fail to note everywhere a tone of helplessness, with perhaps a slight brightening up when the continuous bath is mentioned. The good effect of all the internal remedies may, in almost all instances, be reduced to their tonic or sedative action, and of the external remedies to their soothing effects, their power to diminish tension and burning, or to control the evil odors and the undue activities of the pyogenic bacteria. The treatment, it is true, is still far from our ideal of what effective treatment should be. Nevertheless, we have grounds for claiming that the actual advance made in the treatment of pemphigus is by no means so small as upon first thought it would seem to be. Thanks to Neumann's discovery of the true nature of pemphigus vegetans we are now able to save many a patient from the mental worry and humiliation of being thought to have a syphilitic disease, and from the physical suffering which he would have to undergo before it could be demonstrated by treatment that this diagnosis was incorrect. *Douglass W. Montgomery.*

PENIS, DISEASES OF. See *Sexual Organs, Male, Diseases and Injuries of.*

PENNYROYAL, AMERICAN OR MOCK.—*Hedeoma.* "The dried leaves and tops of *Hedeoma pulegioides* (L.), Pers. (*Mentha p.* L.; fam., *Labiatæ*)." U. S. P.

This is a slender annual herb, very abundant in dry, especially rocky meadows and pastures throughout Eastern and Central North America. The base of the stem is frequently decumbent. The upper portion is usually much branched, the branches are slender, erect or ascending, and quadrangular, the leaves opposite, slenderly petioled; blades usually less than 2.5 cm. (1 in.), long, and 1 cm. (⅜ in.) broad, oblong ovate, narrowed gradually into the petiole, obtuse, distantly and shallowly serrate, pale or grayish-green, thin, with few, strongly ascending secondary veins, and the lower surfaces beset with small, circular, depressed glands, which are usually golden-yellow and shining under a strong lens; flowers several in a leaf axil, pedicelled, the calyx tube cylindraceous, somewhat contracted at the mouth, strongly nerved, its tube two-lipped and slenderly and sharply five-toothed; corolla tubular, two-lipped, pale blue, spotted; stamens four, two of them sterile; odor strong, somewhat mint-like; taste aromatic and pungent.

With a little tannin and bitter extractive it contains nearly one per cent. of a volatile oil, official under the title *Oleum Hedeomæ*, which is its active portion.

American pennyroyal possesses the carminative, aromatic, and diffusive stimulant properties of the mints in general, and is similarly employed. There is no official preparation, but an infusion is probably the best form of administration. One of the important properties of this plant and of its oil is that of repelling mosquitoes, to a considerable and useful extent.

Oil of pennyroyal is thus described: A pale yellowish, limpid liquid, having a characteristic, pungent, mint-like odor and taste. Specific gravity, 0.930–0.940 at 15° C. (59° F.). The oil should form a perfectly clear solution with twice its volume of a mixture of three volumes of alcohol and one volume of water, this solution being neutral or slightly acid to litmus paper. It is also readily soluble in carbon disulphide, or in glacial acetic acid. It consists chiefly of pulegone. The dose is 1–5 minims. The genuine or European pennyroyal is *Mentha Pulegium* L. (*Pulegium vulgare* Mill.) in the same family. It has a similar taste and odor, and contains an almost identical volatile oil. *Henry H. Rusby.*

PENTAL (*Tri-methyl-ethylene*), a purified amylene, introduced by Mering as an anæsthetic. It is a colorless liquid with a sharp penetrating odor, but not irritating to the mucous membrane. Specific gravity, 0.678; boiling point, 100.4° F. It is insoluble in water, but mixes freely with alcohol, chloroform, and ether.

Pental is administered in the same manner as chloroform. Anæsthesia is produced in three or four minutes and lasts for about four minutes.

Following its introduction pental was employed by many as an anæsthetic, with very satisfactory results, but experimental work upon animals proved that it was a powerful cardiac depressant, and also produced marked renal irritation. Many instances of dangerous depression during its use and several deaths were soon reported, and it rapidly fell into disuse. *Beaumont Small.*

PENTASTOMA. See *Arachnida.*

PENTOSURIA is the term applied to the occurrence of sugars of the five-carbon series (pentoses) in the urine. The pentoses ($C_5H_{10}O_5$) include the carbohydrates arabinose, xylose, and rhamnose ($C_6H_{12}O_5$), the latter being a methyl pentose. The appearance of sugars of this type in the urine was first detected by Salkowski and Jastrowitz in the urine of a morphine habitué. Since then similar observations have been made on various individuals. In some of these instances the pentosuria has been found to persist unchanged for many months and even for several years. The pentose either occurs as the only carbohydrate present in noticeable amount, or it may accompany dextrose, the sugar of ordinary glycosuria.

Various methods of testing for pentoses in the urine have been proposed. Of these the following are most widely used:

Tollens' Reaction with Phloroglucin and HCl.—A small quantity of phloroglucin is dissolved in 7–8 c.c. of HCl (specific gravity, 1.12) with the aid of heat. After cooling, ten drops of the urine are added to one-half of the reagent, and the mixture is immersed in a boiling water-bath. In the presence of pentoses a cherry-red coloration quickly results. An immediate spectroscopic examination reveals a characteristic absorption band between the D and E lines. The remainder of the reagent is used for a control comparison with normal urine. The presence of dextrose may interfere with the reaction. (Salkowski's modification.)

Tollens' Reaction with Orcin and HCl.—The urine is mixed with an equal volume of fuming HCl containing orcin (instead of phloroglucin) and heated. After cooling it is shaken with amyl alcohol, which assumes a greenish tint. In this reaction the characteristic spectral absorption band is between C and D. Salkowski prefers the orcin test to all others.

Reaction with Aniline-acetate Paper.—The urine is treated with an equal volume of fuming HCl and heated to boiling. If a strip of filter paper, moistened with aniline acetate, is now immersed in the fluid, it is quickly colored cherry-red by the furfurol formed from the pentoses present.

Liberation of Furfurol by Distillation with HCl.—The method is essentially the same as that used in the estimation of the pentosans in foods. The furfurol may be detected in the distillate by the use of aniline-acetate paper. Normal urine or urines containing dextrose or lactose do not ordinarily give any positive reaction.

Preparation of a Pentosazone.—The osazone is prepared with phenyl-hydrazin and acetic acid as in the ordinary tests for sugar. (See *Urine.*) The pentosazone is characterized by: (1) Its greater solubility as compared with glucosazone; and (2) its melting point, 156°–160° C. When large quantities of dextrose are present, they may previously be removed by fermentation with yeast. The pentoses do not ferment, but they reduce alkaline copper solutions.

Preparation of the Benzoyl Ester.—The benzoyl esters are prepared from 500 c.c. of urine, then saponified with sodium ethylate, and the mixture is filtered at once. The filtrate will give the orcin reaction for pentoses (see above), and glycuronic acid is said to be excluded. When dextrose is present slight modification of the method is desirable. (von Alfthan.)

In considering the possible origin of the pentose found in the urine, the wide distribution of the five-carbon carbohydrates in the vegetable kingdom, as shown by Tollens and others, must be recalled. In the form of pentosans they may enter into the diet. Such precursors of the pentoses occur in certain fruits, like cherries and plums for example. In animal tissues precursors of the pentoses are also found, notably ir the pancreas, from which the carbohydrate may be obtained, combined as a glyconucleoproteïd. Neuberg has shown the pancreas pentose to be *l*-xylose. When fed as such, the pentoses are apparently not well assimilated. Regarding their occurrence in the urine, it seems probable from the meagre data at present available that we must look to metabolic processes for an explanation. For there is no evidence that the diet in the cases on record was particularly rich in pentoses, and in one instance at least pentoses were excreted for a long period on an ordinary diet. Furthermore, the urine pentose is the optically inactive racemic arabinose, and is probably a synthetic product. The pentosuria seems comparable to those perversions of metabolism which are seen in severer forms of diabetes in which the sugar excreted is independent of the diet. In accord with this are the observations of Külz and Vogel on diabetic patients and on dogs suffering from experimental diabetes. They were able to detect pentoses in company with the dextrose present in the urine in several cases. Regarding the immediate precursor of the urine pentose in the body nothing definite is known at present. *Lafayette B. Mendel.*

REFERENCES TO THE MORE IMPORTANT PAPERS ON PENTOSES IN THE URINE.

Salkowski and Jastrowitz: Centralblatt für die medicinischen Wissenschaften, 1892, No. 19, No. 32.
E. Salkowski: Berliner klinische Wochenschrift, 1895, No. 17, p. 364.—Zeitschrift für physiologische Chemie, 1899, xxvii., p. 507.
F. Blumenthal: Berliner klinische Wochenschrift, 1895, No. 26; 1897, No. 12.
Külz and Vogel: Zeitschrift für Biologie, 1896, xxxii., p. 185.
Reale: Jahresbericht für Thierchemie, 1894, xxiv., p. 627.
Colombini: Jahresbericht für Thierchemie, 1897, xxvii., p. 733.
von Alfthan: Archiv für experimentelle Pathologie und Pharmakologie, 1902, xlvii., p. 417.
Bial: Zeitschrift für klinische Medicin, 1900, xxxix., p. 475.
Meyer: Berliner klinische Wochenschrift, 1901, No. 30.
von Jacksch: Zeitschrift für Heilkunde, 1899, xx., p. 195; Deutsches Archiv für klinische Medicin, 1899, lxiii., p. 612. (Alimentary pentosuria.)
Neuberg: Berichte der deutschen chemischen Gesellschaft, 1900, xxxiii., p. 2243. (Nature of the urine pentose.)—*Ibid.*, 1902, xxxv., p. 1472. (Theoretical considerations.)

PENZANCE AND THE SCILLY ISLANDS.—These two localities on the extreme southwestern coast of England, although possessing no great value as health resorts, are taken as representatives of the mild winter marine climate of the south of England. "Penzance appears to be warmer in the winter than any other place on the mainland of England from which we have records" (Dickinson, "Climate and Baths of Great Britain"), and the temperature of the Scilly Islands for the same season is still higher. Mildness and equability of temperature is about all that can be said in favor of such resorts as the above, as well as of others in the same county of Cornwall and in the adjoining one of Devonshire, the most noteworthy of which is Torquay. Such a climate has been resorted to by consumptives and by patients having other inflammatory respiratory affections, notably by those patients with bronchitis who require a moist air.

As will be observed from the climatic chart of Penzance, the temperature range throughout the year is comparatively small. It is neither hot in summer nor cold in winter. Frost and snow are rare. The mean temperature for the three winter months is 43° F., while the mean of the coldest is 40° F. The relative humidity for Penzance is not obtainable, but it probably does not differ much from that at Falmouth, twenty-five miles to the East, which is eighty-two per cent. At the same place (Falmouth) the amount of sunshine is said to be greater than at any other place in England except Jersey, and it is therefore a fair inference that Penzance is also similarly favored, although it is said to have more mist than Falmouth. Everywhere in England there is rain enough, and Penzance, it is seen, has its share, the annual rainfall being 42.59 inches. The winds from the north and south are equally common, while those from the west are more prevalent than those from the east. Penzance has a southeastern exposure, and is sheltered from the prevalent west wind by the high country about the Land's End, and "very completely from the north by elevations of from five hundred to seven hundred feet within four miles. It is exposed, however, to the east, although some protection can be obtained by a choice of residence" (Dickinson, *loc. cit.*). With so many unfavorable climatic features—the large amount of rain; the high humidity; the wind and the relatively small number of sunny days, although large for England—such resorts as Penzance cannot compare with many other mild-winter marine ones except as regards equability; such, for example, as those on the Mediterranean coast, on the Pacific coast of Southern California, on the Gulf and Atlantic coasts of Florida, and many insular resorts. For the inhabitant of England, however, who desires for any reason a mild and equable winter climate, it offers an easily accessible retreat.

CLIMATE OF PENZANCE, ENGLAND. LATITUDE, 50° 8′ NORTH. TEN YEARS.

	January to March.	April to June.	July to September.	October to December.	Year.
Temperature (degrees F.)—					
Mean monthly average	43.2°	52.4°	59.8°	47.7°	50.7°
Mean daily range	6.0	9.7	9.5	6.1	7.8
Mean of warmest	46.3	57.4	64.6	50.6	54.7
Mean of coldest	40.2	47.5	55.0	44.5	46.8
Highest or maximum	58.0	77.0	76.0	64.0	77.0
Lowest or minimum	21.0	33.0	39.0	26.0	21.0
Precipitation—					
Average in inches	10.81	6.65	9.54	15.59	42.59
Wind—					
Prevailing direction	S. W.	N. W.	S. W.	N. W.	S. W.

The situation of Penzance is very picturesque, as indeed are so many of these seaside towns in Cornwall and Devonshire. There are also numerous attractive excursions in the neighborhood and in the adjacent district of Land's End.

The vegetation of Penzance and its neighborhood is very luxuriant and rich, and it seems quite extraordinary that in the latitude of 50°, that of Southern Labrador, one should find exotics flourishing in the open air, even in winter; geraniums and fuchsias attaining the dimensions of large shrubs; aloes flourishing, and hollyhocks, mignonettes, magnolias, and roses blooming, sometimes even in January. Potatoes are cultivated extensively, and sent to London and elsewhere during the winter months. A marked difference is noted between the north and south coasts, although only ten miles apart, not only in the vegetation, but also in the character of the climatic effects. On the north coast the vegetation is far less luxuriant and the climate is more bracing and exciting.

The *Scilly Islands*, although but little resorted to by invalids, represent an interesting phase of climate, and present many attractions from their picturesque situation, as well as from the fact that the Bishop lighthouse, which marks the group, is the first evidence of land which greets the Transatlantic voyager as he enters the English Channel. The group, consisting of forty islands, some only tiny specks, lies about forty miles southwest of Penzance, from which it is reached in four hours. But five islands are inhabited, and but one, St. Mary's, possesses any satisfactory accommodations. This island, which is the largest of the group, contains sixteen hundred acres, and no part of it is a mile from the sea. The scenery is of a peculiar and weird grandeur, great masses of granite cliffs standing out against the sea and storms. In this country the Isles of Shoals, off the New Hampshire coast, would appear to bear a close resem-

blance to the Scillies both in situation, in the open Atlantic, and in their granitic formation and bold rugged scenery. "The air here (Scilly) is as marine as on the deck of an Atlantic steamer. Every sight and sound tells of the sea, the influence of which is here paramount in every shape" (Dickinson, "The Climate of Cornwall," in "Climates and Baths of Great Britain"). The exposed portion of the island of St. Mary's is treeless and bare; but in the valleys, and wherever artificial protection is afforded, the vegetation is luxuriant and almost tropical. Myrtles, fuchsias, geraniums, and aloes grow in great profusion, and palms and bamboo are abundant. "In the gardens of Tresco, unprotected except by the configuration of the ground, a mass of tropical vegetation presents itself which I suppose has no equal in Europe" (Dickinson, *loc. cit.*). The cultivation of the narcissus for Covent Garden is the chief industry of these islands. The climate is relaxing and soothing, a type of a mild, moist, marine one, with great equability. From the chart the mean yearly temperature is seen to be 52.4°, the highest in England. The mean for the three months, January, February, and March is 45.3°. The relative humidity is high, and the rainfall large. The islands are fully exposed to the east and west winds. The former are especially felt in spring. Whatever value such a climate has must consist in its warmth, equability, and humidity, together with the marine influence. About the only conditions which appear to be favorably influenced by such a climatic combination are inflammatory affections of the respiratory organs other than phthisis, especially bronchitis. Chronic renal disease may also do well in such a climate, although the humidity is not a particularly favorable factor. A very charming description of the scenery of the Scilly Islands will be found in Sir Walter Besant's "Amorel of Lyonnesse."

Several other resorts in Cornwall and Devonshire, possessing somewhat similar climatic features, may be mentioned in this connection. On the south coast are Falmouth, Marazion, Torquay, Sidmouth, and other small resorts. On the north coast are St. Ives, Newquay, Tintagel, and Boscastle in Cornwall, and Ilfracombe, Lynmouth, and Lynton in Devonshire. The resorts on the north coast are frequented only in the spring, summer, and autumn.

CLIMATE OF THE SCILLY ISLANDS, ENGLAND, TEN YEARS.

	January to March.	April to June.	July to September.	October to December.	Year.
Temperature (degrees F.)—					
Mean monthly average..	45.3°	52.0°	62.9°	49.7°	52.4°
Mean daily range.....	6.4	8.0	8.0	6.3	7.1
Mean of warmest	48.7	55.9	63.4	53	55.2
Mean of coldest.....	41.8	47.9	55.4	46.7	47.9
Highest or maximum ...	57.0	73.0	75.0	65.0	75.0
Lowest or minimum	29.0	36.0	44.0	32.0	29.0
Humidity—					
Mean relative	87%	84%	85%	85%	85%
Precipitation—					
Average in inches	7.65	5.54	7.52	11.52	32.23
Wind—					
Prevailing direction	W.	N.	W.	W.	W.

Edward O. Otis.

PEPPER, or BLACK PEPPER.—*Piper*, U. S. P.; *Piper Nigrum*, Br. P. The dried, nearly ripe fruit of *Piper nigrum* L. (fam. *Piperaceæ*).

The pepper plant is a native of India, but commercial pepper is wholly the product of cultivated plants, and comes chiefly from the East Indies, that of Penang being preferred. The plant is a woody climber, and is trained chiefly to the betel tree. The fruits are produced in aments, somewhat resembling strings of currants. Upon ripening they turn first red, then yellow. After the latter change their properties are largely lost. They are therefore gathered and dried when they begin to change color.

DESCRIPTION.—About 4 mm. ($\frac{1}{6}$ in.) in diameter, nearly globular, blackish, very strongly reticulate-wrinkled, bearing a low style base at the summit and consisting of a thin fleshy pericarp and a crustaceous, whitish putamen containing a more or less undeveloped seed; odor characteristic, strong; taste strongly aromatic and pungent.

A transverse section of pepper shows a layer of large resin cells near the surface, and beneath this a soft parenchyma (shrivelled in the dry state) containing starch and oil drops. The inner portion of the pericarp contains large oil cells and the seed shows brownish masses of amorphous piperin.

Piper Album, or *White Pepper*, is pepper with most or all of the fleshy portion removed, either before drying or by subsequent grinding. One variety consists of the very young fruit dried entire. Its pungency varies accordingly. If nearly ripe when gathered, it is less pungent than it is when the innermost layers of the sarcocarp have been rubbed or ground away, since these are rich in the active constituent.

COMPOSITION.—The pungency of pepper is due to the presence of ten or twelve per cent. of soft, very sharp-tasting *resin*, which is contained, as indicated above, mostly in the cells just beneath the surface. An *essential oil* of clear white color, having the full fragrance of the spice without its biting taste, exists to the extent of one or more per cent. The third and most peculiar ingredient is the neutral, crystalline, tasteless, and inodorous substance *piperin*, which exists to the extent of from two to eight per cent. It was discovered by Oerstedt in 1819. Piperin is scarcely soluble in water, but dissolves moderately well in chloroform, ether, and alcohol; at 212° F. it melts to a yellow, oily liquid. Besides these, starch, mucilage, and albuminous matters are found, as in other vegetable tissues.

ACTION AND USE.—Applied to the skin, pepper is rubefacient, and finally painfully irritant. It is occasionally sprinkled over the surface of other applications for this effect. In water it is a popular but painful gargle for "sore throat." Taken internally, it is in small doses a stimulant, in large ones an irritant to the stomach—that is, it acts like most other spices. It has been given as a specific in the treatment of hemorrhoids, but is out of use for this purpose. As an antiperiodic it is also obsolete, although piperin is occasionally mentioned in this connection. Whole peppers were formerly swallowed for the cure of some cases of dyspepsia. Dangerous symptoms—"rigors, convulsions, and delirium"—have been said to follow the immoderate use of pepper (Phillips). Although a typical spice, pepper is much less employed in medicine than ginger, cardamon, and cinnamon.

ADMINISTRATION.—For dyspeptics or others needing spices, there is no better way than to eat it on the food, or if a larger quantity is indicated than is agreeable to the taste, 0.5 gm. (gr. vij.) or less may be given in pills or in a bolus, with honey, two or three times a day; or four or five drops of the *oleoresin* (*Oleoresina Piperis*, U. S. P., strength about $\frac{5}{1}$) may be taken if a more compact and stronger dose is needed. Dose of piperin, 0.5 gm. or less.

ALLIED PLANTS.—The genus is a very large one, of six hundred species, of exclusively tropical plants, mostly shrubs, and frequently, like the present one, climbers. Many of them have pungent fruits. *P. officinarum* Cas., D. C., and *P. longum* Linn., are the sources of "long pepper," which comes in compact spikes one or two inches (2–5 cm.) long, and about a sixth (0.5 cm.) in diameter. Its constituents are identical with those of the above, but its flavor and strength are inferior. Long pepper is never sold at retail in this country, yet it is a common article in wholesale houses; it is probably used as an adulterant of black pepper. *P. betlé* Linn. is an East Indian vine whose leaves are chewed with areca nuts as a masticatory (or a habit) by many aboriginal tribes of the great Polynesian Islands (see also *Cubeb*, *Matico*, and *Kava*).

W. P. Bolles.

PEPPERMINT.—*Mentha Piperita.*—"The dried leaves and tops of *Mentha Piperita* L. (fam. *Labiatæ*)," U. S. P.

Peppermint is a slender, nearly smooth, perennial herb, native of Europe, widely naturalized in temperate regions and cultivated upon a great scale for the herbage, for culinary uses, for flavoring and perfuming, for medicinal employment, and for the distillation of its oil and the preparation of menthol. It spreads by runners, producing frequently dense beds of slender stems about a yard long, ascending from a prostrate rooting base, quadrangular, frequently purplish, and bearing leaves and flowers described below. The stems and leaves are very sparingly and obscurely hairy, the hairs short and stout, usually containing menthol crystals in one or more cells; leaves opposite; exstipulate, petioled, the petioles winged toward the summit, the blades usually less than 5 cm. (2 in.) long and about half as broad, ovate, with the rounded base very abruptly produced into the petiole, acute, sharply serrate, thin, wrinkled, of a bright and usually light green; flower spikes oblong or oval, 1–2 cm. ($\frac{2}{3}$–$\frac{3}{4}$ in.) broad, with rounded summit, dense, or somewhat interrupted at the base; flowers about 6 mm. ($\frac{1}{4}$ in.) long, the calyx tubular, ten-nerved, scarcely two-lipped, five-toothed; corolla light purple, nearly equally four-lobed, or one lobe (consisting of two united) a little larger; stamens four, short, equal; fruit of four ovoid, smooth nutlets; odor strong, but not heavy, characteristic; taste characteristic, pungent, and cooling.

The leaves bear numerous globular oil glands and slender, several-celled hairs which often contain menthol crystals.

The drug contains, with a little tannin, about one per cent. of a volatile oil, which is the active constituent, is official under the title *Oleum Menthæ Piperitæ*, and is described as follows in the Pharmacopœia:

A colorless, yellowish, or greenish-yellow liquid, becoming darker and thicker by age and exposure to the air, having the characteristic, strong odor of peppermint, and a strongly aromatic, pungent taste, followed by a sensation of cold when air is drawn into the mouth.

Specific gravity, 0.900–0.920 at 15° C. (59° F.).

The oil does not fulminate with iodine.

It forms a clear solution with an equal volume of alcohol, becoming turbid when somewhat further diluted, and is soluble, in all proportions, in carbon disulphide, and in glacial acetic acid.

The alcoholic solution of the oil is neutral to litmus paper.

If five drops of the oil be added to 1 c.c. of glacial acetic acid, and the mixture gently warmed, the liquid will assume a blue color, with a red fluorescence.

If 2 c.c. of the oil be mixed with 1 c.c. of glacial acetic acid, and one drop of nitric acid added, the liquid will soon acquire a green, greenish-blue, blue, or violet tint with a copper-red fluorescence.

If 1 c.c. of the oil be dissolved in 5 c.c. of alcohol, 0.5 gm. of sugar and 1 c.c. of hydrochloric acid added, and the mixture gently heated, a deep blue or violet color will gradually be produced.

If to 5 c.c. of nitric acid one drop of the oil be added, and the mixture gently agitated, and allowed to stand for about three hours, it should have a yellowish, but not a bright red, color (absence of *oil of camphor* and of *oil of sassafras*).

If a portion of the oil, contained in a test tube, be placed in a freezing mixture of snow (or pounded ice) and salt for fifteen minutes, it should become cloudy and thick, and after the addition of a few crystals of menthol, being still exposed to cold, it should soon form a crystalline mass (distinction from *dementholized oil*).

When heated on a water-bath, in a flask provided with a well-cooled condenser, the oil should not yield a distillate having the characters of *alcohol*.

This oil contains as its active portion the peculiar substance *menthol*, considered separately under that title. A good article has been found to contain about sixty per cent. of total menthol, about one-fourth of it occurring as ester, the remainder free. However, the percentage and composition of the oil, as produced in different countries, and even in different parts of the same country, varies widely, not only as to the percentages, but even as to the nature, of the compounds.

ACTION AND USE.—Notwithstanding that menthol is the active constituent of peppermint and its oil, yet the action and uses of the latter and of that constituent require separate consideration.

Peppermint and its oil are, from their taste and agreeable action, the most generally liked of all the mints, if

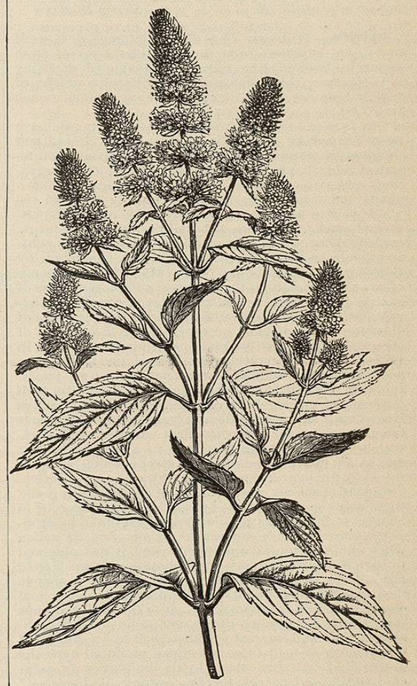

FIG. 3793. — Peppermint Plant. About one-half natural size. (Baillon.)

not of all carminatives. This oil is warming and stimulating to the stomach, very seldom irritating. It is a favorite household remedy for nausea, flatulence, and colic; applied to the skin and evaporation prevented, it is a mild stimulant, useful in neuralgia and rheumatism; applied to the forehead and temples it produces a grateful, cooling feeling, with a little tingling that occasionally relieves slight headaches; this property is mostly due to the menthol it contains. The most common employment of peppermint oil by physicians, however, is as a flavor, vehicle, or adjuvant of other medicines, especially of cathartics, whose griping it undoubtedly diminishes. Like most mints, peppermint is frequently used in hot infusion in colds, etc. It is also a favorite flavor for candies.

The powdered drug is sometimes given in doses of 1–2 gm. (gr. xv.–xxx.). There is, properly speaking, no

official preparation of it, though the official spirit contains one per cent. It is often given in the form of the infusion. The common form of administration is that of the oil (dose 1–5 m.), or of the following preparations of it: The Spirit or Essence (*Spiritus Menthæ Piperitæ*) contains ten per cent. of the oil, and there is three and a half per cent. of it in the popular mixture of rhubarb and soda. The dose of the spirit is 0.3–1 c.c. (♏ v.–xv.). Peppermint water (*Aquæ Menthæ Piperitæ*) contains 0.2 per cent. of the oil and is given in doses of 15–60 c.c. (fl. ℥ ss.–ij.). The official troches each contain 0.01 c.c. (about ♏ $\frac{1}{6}$) of the oil. *Henry H. Rusby.*

PEPSIN.—*Pepsinum, U. S. P.* "A proteolytic ferment or enzyme obtained from the glandular layer of fresh stomachs from healthy pigs, and capable of digesting not less than three thousand times its own weight of freshly coagulated and disintegrated egg albumen when tested by the process given below."

Our present knowledge and conception of pepsin have been arrived at by the inevitable, slow, intermittent progress in science, marked by brilliant epochs and retarded and clouded by faulty and incomplete observations and erroneous theories. The investigation of ferments and ferment action has necessarily involved the whole field of problem and inquiry in biology. The history of pepsin, therefore, is found in the voluminous recorded labors of a host of workers. In briefest possible mention it begins perhaps with the first perception by Borelli, three centuries ago (1608–1679), of the existence of secreting glands in the stomach and of the value of gastric juice; then the studies of the gastric juice of regurgitating birds, which established the independence of digestion of mechanical power (an early theory) and of chemical change produced on food (Réaumur, 1752). In 1772 Hunter's observations established the fact of the post-mortem digestion of the stomach by its own juices. It was in 1783 that the first demonstration *in vitro* with pure animal gastric juice obtained by ingenious devices from living animals (Spallanzani) was made. At about this time also were made the first recorded clinical researches in regard to gastric juice as a surgical solvent and as an internal remedy—researches which were inspired by Spallanzani and made by his colleagues, Jurine, Carminati, Senebier, and others. Many interesting and singularly clear and detailed observations are recorded in relation to the gastric juice of beasts and birds, its properties, behavior with various foods, etc., and its action when used as a topical application; and it was observed to have the power "to remove all disagreeable smell from fetid ulcers, to give them a clean appearance, to change the quantity and quality of suppurative matter, and obtain a speedy cicatrization." It was employed thus successfully for tumors, ulcers, gangrene, old sores, abscesses, etc., and internally with benefit in "weakness of the stomach and all those affections produced by faults in this fluid and particularly by its diminution in point of quantity and energy for the purpose of digestion." Very remarkable effects were particularly noted in a "case of gradual emaciation with continual nausea and vomiting."

In 1824 Prout, Tiedemann, and Gmelin discovered hydrochloric acid in the gastric juice. In 1834 Beaumont made his classical observations, and drew the faulty conclusion that gastric juice was the sole digestive fluid and formed gastrites with food. In the same year an impetus was given to the study of gastric juice by Eberle's suggestion and use of infusions from the stomach glands. This led to the brilliant and careful researches of Schwann (1836) upon the active principle of the gastric juice—its behavior, theory of action, method of separation, etc. He gave to this principle the name "pepsin." In 1842 Lehmann published his theories as to the protein nature and cellular origin of pepsin, and its action in the transformation of albuminoids into absorbable substances. Wasmann also put forward at the same time the theory that pepsin is the granular matter of the cell or the substance from which it is formed. In 1857–58 Corvisart and Beale suggested the use of pepsin itself in medicine. In 1864 Hoppe-Seyler classified the various forms of proteids according to their solubility and precipitability by various neutral alkali salts, this classification, by reason of the similarity of pepsin in these respects to other proteids, leading to the present methods by which pepsin is produced by these reagents. Scheffer's suggestion and development of sodium chloride as a pepsin precipitant were inspired by his observations of this reaction of proteins.

Pepsin is now produced from the stomach with the same facility as quinine is made from bark; for, in view of its peculiar origin and nature and susceptibilities on the one hand, it is singularly capable of extraction and utilization in a practical way as an article of commerce. During the last half of the twentieth century, with its accurate, scientific methods of research, and especially during the past thirty years in which pepsin has been increasingly utilized, it, as well as the gastric extract and gastric juice itself, has been the subject of elaborate investigation, and we have now exhaustive data concerning pepsin from a pharmaceutical standpoint.

Great therapeutic interest attaches to the very recent methods of Pawlow for obtaining pure gastric juice from the living animal (dog), to his profound studies thereof, and to the free administration, by Fremont and his colleagues, of this juice in cases of disease of the stomach. They gave it in quantities that sometimes amounted to as much as 500 c.c. per day, and the results which they obtained were at times brilliant. They also used gastric juice as a topical application, noting its solvent, healing and sedative action; this latter quality was also attributed to it when administered internally. Fremont considers this animal gastric juice to be especially adapted to all cases of hyposecretion of the stomach, whether resulting from glandular ulceration, from acute or chronic infection, or from disease of the liver, heart, lungs, and nerve centres. Under its influence dyspeptic phenomena have disappeared more or less promptly, and a remarkable gain in weight and strength has taken place. Patients who have suffered acutely from dyspepsia, and who have become extremely emaciated, have also obtained complete and permanent relief under the use of the remedy.

Pawlow especially calls attention to the fact that gastric juice is now pharmaceutically available as a clinical agent. Others have argued that with a corresponding free use of pepsin and acid similar results may be obtained.

Inasmuch as the healthy stomach of recently killed animals affords a resource for gastric juice in a very concentrated form, rendered perfectly pure by simple means of clarification and filtration, sterile, and free from objectionable odor and taste, there is good ground for the presumption that the fullest therapeutic possibilities of the gastric juice may be realized without the elaborate methods resorted to in obtaining the secretion from the living animal. These observations, which represent the last word of modern achievement in this particular field, give great interest and significance to the early discoveries of Spallanzani and his colleagues, and to the fact that they attracted no further attention and were thus barren of result.

Pepsin is found in the gastric cells of all animals, but the gastric juice of the carnivora is much more powerful in proteolytic action. Pepsin itself, however, has no particular degree of energy or peculiarity of action from any particular source; its "strength" is strictly in ratio to its degree of isolation from the associated non-peptic material of the gastric cell or juice, and from the agents used in its separation therefrom. The pepsin obtained from one creature, therefore, is not stronger than that obtained from another. In the gastric juice of the dog, it is to be noted that the pepsin is associated with a peculiarly high percentage of HCl.

Pepsin is normally associated also with another distinct ferment—the milk-curdling enzyme—which is very energetic in the suckling animal. The ultimate composition of pepsin, the method of its elaboration from the cell, the

mode of its action, and its relation to the other constituents of the gastric juice, proteid, hydrochloric acid, and inorganic salts, have been the subject of laborious research and of speculation, and are receiving increased attention in the progress and practical interest of biological study.

Pepsin is a soluble, unorganized ferment, an enzyme, having the property of converting native proteids into soluble, highly diffusible, non-coagulable proteids. Its action is exerted only in an acid medium, most freely in the presence of 0.2 per cent. absolute acid, slight variations from this not sensibly influencing its action; if the proportion of acid, however, be materially increased—say, to 0.3 per cent.—the enzyme is much enfeebled.

Pepsin exerts freely its characteristic action in the presence of organic acids in general—lactic, tartaric, citric, etc. Notwithstanding the fact that the ferment is so closely and characteristically related to the HCl, the mineral acids in general are not favorable to its action, phosphoric being the only one which approximates at all to the HCl in its affinity to the enzyme; nitric and nitro-muriatic acids are distinctly unfavorable.

Pepsin exhibits considerable activity at a temperature much below the physiological, converting albumen slowly even at ordinary room temperature (60°–70° F.), and its action is completely arrested only at a temperature of about 40° F., and greatly accelerated at 120°–130° F.

Pepsin does not exist preformed in the gastric cell, but is developed from the mother substance, pepsinogen, and under the influence of the acid simultaneously secreted in the gastric juice. This view has for a long time been entertained, and very recently pepsinogen has by Glaessner been prepared free from pepsin and found to be devoid of proteolytic power. This pepsinogen was found promptly to develop into pepsin under the influence of both mineral and organic acids; while oxygen and neutral salts were without effect, and alcohol, ether, and chloroform proved destructive.

"If it be desired to use a diluent for reducing pepsin of a higher digestive power to that required by the Pharmacopœia, sugar of milk should be employed for this purpose.

"A fine, white, or yellowish-white, amorphous powder, or thin, pale yellow or yellowish, transparent or translucent grains or scales, free from any offensive odor, and having a mildly acidulous or slightly alkaline taste, usually followed by a suggestion of bitterness. It slowly attracts moisture when exposed to the air.

"Soluble, or for the most part soluble, in about one hundred parts of water, with more or less opalescence; more soluble in water acidulated with hydrochloric acid; insoluble in alcohol, ether, or chloroform.

"On heating a solution of pepsin in acidulated water to 100° C. (212° F.) it becomes milky, or yields a light, flocculent precipitate, and loses all proteolytic power. In a dry state it can bear this temperature without injury.

"Pepsin usually has a slightly acid reaction. It may be neutral, but should never be alkaline."

Pepsinum Saccharatum, U. S. P.—"Pepsin triturated with milk sugar in such proportion that the resultant saccharated product shall digest three hundred times its own weight of coagulated egg albumen under the United States Pharmacopœia method of valuation for pepsin."

Pepsin of the British Pharmacopœia is of 1–2,500 strength. The United States Pharmacopœia method of valuation (that of the British Pharmacopœia is similar) in brief is this: 0.003 gm. of pepsin is required completely to digest 10 gm. of hard-boiled comminuted egg albumen in 100 c.c. of a 0.2-per-cent. solution of absolute HCl in distilled water, the mixture maintained at a temperature of 100°–104° F. for six hours, and the flask shaken gently every fifteen minutes. At most only a few thin, insoluble flakes should be left. Pepsin fluids must be assayed according to the United States Pharmacopœia method, the conditions prescribed being strictly adhered to, but use being made of a corresponding proportion of the fluid to represent the amount of ferment necessary to digest the 10 gm. of albumen.

Pepsin of the United States Pharmacopœia and British Pharmacopœia requirements is obtained by precipitation, with neutral salts, of the alkalies from purified infusions of the fresh, healthy stomach glands, and the precipitate purified by mechanical means—by reprecipitation and dialysis. By this means mucus is wholly, and non-peptic proteids and peptones well, separated. The *rationale* of the process will appear in the consideration of the nature and behavior of the enzyme.

No official method is given in the United States Pharmacopœia or in the British Pharmacopœia; their standards make obsolete the cruder, earlier forms. It is to be regretted that European standards are so greatly inferior, for a uniform, definite, adequate pharmacopœial standard for pepsin of commerce is absolutely essential. In the past pepsin has been too commonly of insignificant value—even inert; and variable and apparently conflicting results and theories are inevitable when pepsin still means in various countries a product of from 1 to 40 to 1 to 3,000 standard; moreover, there are offered in commerce, in the United States, pepsins of even *stated* digestive value below the obligatory pharmacopœial standard.

Both physiological and chemical data almost irresistibly lead to the conclusion that pepsin is a nucleo-proteid and sharply distinguished from all other forms of proteid by its proteolytic action, exhibited under conditions which are in themselves incapable of effecting these chemical changes without the intervention of the enzyme. The degree of isolation of pepsin is necessarily only to be judged by the energy of the product which is obtained by the exclusion of foreign substances capable of separation and identification by chemical processes and dialysis. The enzyme so far isolated exhibits the characteristic behavior of a nucleo-proteid. It is freely soluble in water, is non-dialyzable, readily precipitated by the neutral salts of the alkalies and by strong alcohol in excess, and is coagulated in solution at 160° F. both in neutral and in acid media; it is destroyed in solution at this temperature (160° F.) which, it is interesting to note, is the coagulating point of albumen and destructive to organized ferments; it is destroyed in alkaline solutions at any temperature; its action is strongly influenced by various reagents which do not in themselves effect any known change in the enzymic substance; and, finally, when once destroyed its vitality cannot be restored by any means whatever. A striking example of its physiological relations is found in its behavior with common salt; the presence of sodium chloride in so small a quantity as one per cent. of the digesting mass completely retards digestion *in vitro*, yet we have the fact that pepsin may be precipitated by means of common salt (in saturated solution), and kept in contact with it for a long time without impairment of its activity.

The most perfectly isolated pepsin yet produced is found to be a nitrogenous body with the chemical constitution of a proteid, and this pepsin-proteid contains phosphorus and iron like other nuclein bodies. The fact, then, that the chemical composition of pepsin remains yet to be absolutely established is of little significance from a therapeutic standpoint, for it imposes, in the light of all the material and important facts known, no limitations upon the complete utilization of the enzyme.

The physiological test for pepsin is as conclusive and reliable as any chemical test by which we establish the presence or identity of any chemical substance. It is by the physiological test that we readily measure the strength of any specimen of pepsin; and it is by it, furthermore, that we have determined the influence of medicinal and food substances upon pepsin, and have gained accurate data as to the conditions which are favorable and unfavorable to its action or destructive to the life of the enzyme. These data clearly reveal that physiological considerations are as conclusive in relation to the enzymes as are chemical reactions, both in theory and in practice, in relation to the use of other agents of the materia medica.

Pepsin behaves as a true ferment whose peculiar form