GELATIN IN MEDICINE.*

BY GEORGE D. BEAL[1] AND ANDREW NEFF.[2]

HISTORY OF GELATIN.

The first extensive use of gelatin was during the French revolution. The French government, backed by the Academy of Medicine, supplied the poor with gelatin soups. Bulletins were issued which stressed the value of these soups and recommended their use in place of the prevalent beef teas, but this new product of the soup kitchens was viewed with some suspicion by the citizens.

At about this time a French gelatin manufacturer, named Gannal, decided to make use of his family in deciding upon the food value of gelatin. They endured for some time the gelatin with bread and water diets which Gannal prepared, then their health began to fail. Not understanding at that time the significance of unbalanced diets, these experiments necessarily led to unsatisfactory results.

The first scientific work of definite value was probably that of Carl Voit in Munich about the year 1870. Voit's conclusion, still applicable, was that gelatin always spares protein, and to a greater extent than either fat or carbohydrate. Gelatin is an incomplete protein, however, and hence cannot be used as the sole source of protein supply.

MANUFACTURE OF GELATIN.

Edible gelatin is prepared commercially by steam-cooking specially prepared bones or skin. The material is first thoroughly washed, then limed for some 30 or more days, rewashed, neutralized and heated in open vessels by means of steam coils. This process breaks down the original proteins, casein or collagen, into gelatin. After the gelatin solution has been concentrated, filtered and clarified, it is allowed to gel, and is then dried and ground to about 30-mesh. The final product contains about 12 per cent of water. The better grades of American edible gelatin easily conform to, and some of them exceed, the purity requirements of U. S. Pharmacopœia X.

GELATIN AMINO ACIDS.

Table I shows the amino acids found in the gelatin molecule and in the molecules of casein, gliadin, zein, hordein and prolamin (taken from Sherman's "Chemistry of Food and Nutrition").

The proteins have a slightly higher caloric value (an average of 5.65 Calories[3] per gram) than the carbohydrates (an average of 4.1 Calories per gram), due to their higher content of carbon and their lower content of oxygen. In other words, they are in a less highly oxidized condition than the carbohydrates. The fats are still less oxidized and correspondingly show a still higher caloric value (an

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[3] Calorie when spelled with a capital "C" indicates the amount of heat necessary to raise 1000 grams of water from 0° to 1° C. When spelled with a small "c," the amount of heat necessary to raise one gram of water from 0° to 1° C.

average of 9.45 Calories per Gm.). These points are well brought out by Table II, also taken from Sherman's "Chemistry of Food and Nutrition."

TABLE I.

	Gelatin.	Casein (milk).	Gliadin (wheat).	Zein (corn).	Hordein (barley).	Prolamin (rye).
Glycine	25.50	0.45	0.00	0.00	0.00	0.13
Alanine	8.70	1.85	2.00	13.89	0.43	1.33
Valine	1.00	7.93	3.34	1.88	0.13	?
Leucine	7.10	9.70	6.62	19.55	5.67	6.30
Proline	9.50	7.63	13.22	9.04	13.73	9.82
Oxyproline	14.10	0.23	?	?	?	?
Phenylalanine	1.40	3.88	2.35	6.55	5.03	2.70
Glutamic acid	5.80	21.77	43.66	26.17	43.20	38.05
Oxyglutamic acid	0.00	10.50	2.40	2.50	?	?
Aspartic acid	3.50	4.10	0.58	1.80	?	0.25
Serine	0.40	0.50	0.13	1.02	?	0.06
Tyrosine	0.01	6.50	3.50	3.55	1.67	1.19
Cystine	0.31	0.50	2.32	0.85	1.55	?
Histidine	0.90	2.84	3.35	0.82	2.14	0.39
Arginine	8.22	3.81	3.14	1.82	2.89	2.22
Lysine	5.92	7.62	0.92	0.00	1.01	?
Tryptophane	0.00	2.20	1.14	0.00	1.05	Present
Ammonia	0.49	1.61	5.22	3.64	4.84	5.11
Summation	92.85	93.62	93.89	92.58	83.34	67.55

TABLE II.

	Heat of Combustion in calories per Gm.	Per cent of carbon.	Per cent of hydrogen.	Per cent of oxygen.	Per cent of nitrogen.
Sucrose (cane sugar)	3.96	42.1	6.4	51.5	0
Starch, glycogen	4.22	44.4	6.2	49.4	0
Butter fat	9.30	75.0	11.7	13.3	0
Gliadin	5.74	52.7	6.9	21.7	17.7
Casein	5.85	53.1	7.0	22.5	15.8
Gelatin	5.30	50.0	6.6	24.8	18.0

Glycine, the amino acid present in largest amount in gelatin, is one of the substances used by the body in detoxicating materials of the benzene type, such as phenyl acetic acid, phenols and cresols. According to A. P. Mathews[1] the formation of glycocholic acid in the bile may be a similar process, since cholic acid is decidedly toxic.

Alanine like glycine can probably be synthesized by the animal organism.

Lysine and proline are both necessary for the growth of animal organisms. When present in small amounts only, health can apparently be maintained, but growth is inhibited.

Tryptophane apparently cannot be synthesized by the animal organism, and its absence, as well as the absence of oxyglutamic acid from the gelatin molecule, put this protein in the incomplete class. Tryptophane is responsible for the formation of indol and consequently of indican in the indican test for putrefaction.

[1] "Physiological Chemistry," 4th Edition.

Tryosine is practically absent from the gelatin molecule, but this amino acid can apparently be synthesized from phenylalanine, which is a matter of introducing an hydroxyl group.

GELATIN AS A PURE PROTEIN.

Gelatin like many other proteins belongs to the "incomplete" class; *i. e.*, it cannot supply all the amino acids which the body requires (tryptophane and oxyglutamic acid are practically absent). However, as can be seen in the above table, it does contain a considerable variety of these acids.

It is of interest to note here that, since gelatin is prepared by simple hydrolysis of ossein or collagen (the proteins found in bone, tendon, etc.), in supplying these particular organs with amino acids, gelatin probably acts as a "complete protein." But while gelatin cannot meet all of the protein requirements of the body, Kirchmann[1] has shown that if 12 per cent of the bodily energy requirements are supplied by gelatin, the decomposition of body protein, or the requirement of other proteins as foods, is lessened by 27 per cent.

The amino acids present in the gelatin molecule are in a readily accessible form; *i. e.*, gelatin is a very easily digested protein.

GELATIN IN INFANT FEEDING.

Gelatin shows much promise as an infant food, especially as a milk diluent in infant formulas. Its use in this connection goes back many years. J. Alexander,[2] P. B. Hawk,[3] T. B. Downey,[4] believe that the rôle played by the gelatin is that of a protective colloid, modifying the curd formation of the casein during digestion. R. M. Washburn[5] and also L. S. Palmer and G. A. Richardson[6] find no evidence of such an action. Work that we have done in attempting to ascertain the part played by gelatin in enhancing the availability of cow's milk, has given nothing of clear value. While there is probably little or no influence of gelatin upon the size and rate of formation of casein curds, the texture of the curds formed is still an open question, and may be a matter of some moment. At the present time we are conducting some experiments in coöperation with the Children's Hospital of Pittsburgh and the Knox Gelatine Company, by means of which we hope to acquire pertinent information of dietetic interest.

Last summer we carried out some tests in which nine members of Mellon Institute subsisted for about one month on plain and gelatinated milks. With the exception of a small amount of fruit, no other food was taken. We were not able to draw definite conclusions as to the relative merits of plain and gelatinated milk from these tests; but it is interesting to note that, in spite of what would generally be considered a strenuous diet, these men all continued their work as usual, and all remained in perfect health throughout the test.

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[1] *Z. Biol.*, 40 (1900), 54.

[2] *J. Am. Chem. Soc.*, 32 (1910), 680–87.

[3] *Proc. Soc. Exptl. Biol. Med.*, 20 (1923), 269.

[4] *J. Metabolic Research*, 5 (1924), 145.

[5] *Vermont Agri. Expt. Station Bul.* (1916), 195.

[6] 3rd Colloid Symposium, 1925.

HEMOSTATIC ACTION OF GELATIN.

Gelatin has been used as a hemostatic agent in China and Japan since prehistoric days. Its use for this purpose has persisted in Europe and in this country, although occasional cases of tetanus developed early in the history of the treatment when improperly sterilized solutions were used hypodermically. Perhaps, also, the gelatin employed was an inferior, unsuitable product.

The rôle played by the gelatin as a styptic is still uncertain. There are those who claim that the action is due to the calcium content, as gelatin is sometimes spoken of as a calcium gelatinate. Others maintain that the action is attributable to some organic function of the protein molecule.

According to H. C. Wood,[1] partly digested gelatin or gelatose is just as effective a styptic as is gelatin itself. This finding seems to suggest that gelatin given by mouth is as effective (although slower) as gelatin given hypodermically, other conditions being equal.

In regard to the effectiveness of gelatin as a styptic, Grau[2] injected 25 to 40 cc. of a 10 per cent solution of Merck's sterilized gelatin, and noted an increase in the coagulability of the blood two to four hours after the injection. A maximum effect was reached ten to twelve hours after the injection. He found the degree of increased coagulability to vary in different experiments from 66 per cent to 85 per cent. The effect continued unabated for several hours.

A report of Vossmer is of unusual interest in this connection. He found in some thirty gelatin-fed cases of melena neonatorum (greater or less amounts of blood in the fæces of the new-born) a mortality rate of 8.8 per cent. A previous mortality rate was 61.3 per cent in some thirty cases.[2]

THERAPEUTIC USES OF GELATIN.

The therapeutic uses of gelatin in general include its use in cases of internal or external hemorrhage, as epistaxis, bleeding from hemorrhoids, gastric ulcer (180 cc. of a 10 per cent solution twice in 24 hours), and hemorrhage from the bladder. The latter is treated by injecting sterilized gelatin.

The subcutaneous use of gelatin is indicated in hemorrhages such as hematemesis, metrorrhagia, melena neonatorum, and the purpuric forms of the infectious diseases, and is contra-indicated only in acute nephritis and parenchymatous renal hemorrhage.[3]

GELATIN AS A BASIS FOR CAPSULES AND SUPPOSITORIES.

Pharmacists are all familiar with the use of gelatin in the preparation of court-plaster, capsules, suppositories, lozenges, disks, etc. Gelatin in sheet form, having an appropriate glycerin content, yields itself admirably to the mass production of flexible capsules, or pearls, for the administration of oily medicaments. The coating of pills with gelatin is too familiar to warrant discussion here.

The plain gelatin capsules digest readily, so liberate their contents in the stomach. Capsules treated with formaldehyde, the so-called enteric capsules,

[1] *Am. Med.* (May 3, 1902).

[2] *Deut. med. Wochschr.* (1910), No. 27.

[3] Sajous' "Analytic Cyclopaedia of Practical Medicine." It has been used subcutaneously, in the treatment of aneurisms (by Lancereaux and Osler).

however, do not digest until they reach the intestine, so that their contents are liberated farther down.

Glycerinated gelatin suppositories (1/3 gelatine, 1/3 glycerol, 1/3 water), nasal, urethral, rectal and vaginal, are used in large quantities. They are firm, yet contain relatively large quantities of water, in which can be dissolved various medicaments.

GELATIN IN ADULT DIETARIES.

Gelatin is used in the adult dietary primarily in the form of salads and desserts, making the many attractive dishes with which all are familiar. Its use in the manufacture of ice cream is practically universal; about 0.5 per cent of gelatin is used and gives the cream a smooth velvety texture. The great advantage of gelatin in special dietaries, especially those for use in hospitals, lies in the fact that it is a pure protein, of known caloric value, making it a simple matter to calculate formulas, readily assimilable, and easily combined with practically any other form of foodstuff, especially vitaminous foods of value in the various so-called deficiency diseases. The above-mentioned quality, that of adding attractiveness to dishes, is of particular importance in preparing special foods for invalids and convalescents, where, for psychological reasons, the appetite must be tempted in every way possible.

PITTSBURGH, PA.

PRESCRIPTION CLINIC.*

BY ADLEY B. NICHOLS.

An introduction is hardly necessary for this clinic, as it has been conducted often enough for most of you to know its plan and purpose. All prescriptions presented are authentic and have been collected during the past year from current files. Many of those obtained were duplicates or have been presented before, and a large number of those brought to my attention as incompatibilities seem to offer no trouble or difficulty when compounded just as written, no matter how many times they were tried. In other words it would seem to show undue carelessness on the part of the original compounder, either as to the method of procedure or the ingredients used in filling the prescription. Prescriptions are printed as written.

℞ 1	Tr. Aconit.	*f*ʒ *ii*
	Tr. Bellad.	*f*℥ *i*
	Sod. Brom.	℥ *i*
	Elix. Pepsin. et Bismuth *q. s.*	*f*℥ *vi*

M ft. sol.

In this prescription, the bismuth is immediately precipitated by the sodium bromide; in the form, however, of a very creamy milk, which readily stays in suspension upon shaking. All that is required is a "shake label."

℞ 2	Stront. Salicyl.	ʒ *iv*
	Sod. Bicarb.	ʒ *iv*
	Phenyl. Salicyl.	ʒ *ii*
	Elix. Aromat. *q. s.*	*f*℥ *iii*

* Prescription Clinic of Section on Practical Pharmacy and Dispensing, A. PH. A., St. Louis meeting, 1927.