GELATIN

1. Introduction

Gelatin [9000-70-80] is a protein obtained by partial hydrolysis of collagen, the chief protein component in skin, bones, hides, and white connective tissues of the animal body (see COLLAGEN). Type A gelatin is produced by acid processing of collagenous raw material; type B is produced by alkaline or lime processing. Because it is obtained from collagen by a controlled partial hydrolysis and does not exist in nature, gelatin is classified as a derived protein. Animal glue and gelatin hydrolysate, sometimes referred to as liquid protein, are products obtained by a more complete hydrolysis of collagen and can thus be considered as containing lower molecular-weight fractions of gelatin.

Use of animal glues was first recorded ca 4000 BC in ancient Egypt (1). Throughout subsequent centuries, glue and crude gelatin extracts with poor organoleptic properties were prepared by boiling bone and hide pieces and allowing the solution to cool and gel. Late in the seventeenth century, the first commercial gelatin manufacturing began. At the beginning of the nineteenth century, commercial production methods gradually were improved to achieve the manufacture of high molecular weight collagen extracts with good quality that form characteristic gelatin gels (1–3).

Uses of gelatin are based on its combination of properties: reversible gel-to-sol transition of aqueous solution; viscosity of warm aqueous solutions; ability to act as a protective colloid; water permeability; and insolubility in cold water, but complete solubility in hot water. It is also nutritious. These properties are utilized in the food, pharmaceutical, and photographic industries. In addition, gelatin forms strong, uniform, clear, moderately flexible coatings which readily swell and absorb water and are ideal for the manufacture of photographic films and pharmaceutical capsules.

2. Chemical Composition and Structure

Gelatin is not a single chemical substance. The main constituents of gelatin are large and complex polypeptide molecules of the same amino acid composition as the parent collagen, covering a broad molecular weight distribution range. In the parent collagen, the 18 different amino acids are arranged in ordered, long chains, each having ~95,000 mol wt. These chains are arranged in a rod-like, triple-helix structure consisting of two identical chains, called α_1, and one slightly different chain called α_2 (4–6). These chains are partially separated and broken, ie, hydrolyzed, in the gelatin manufacturing process. Different grades of gelatin have average molecular weight ranging from ~20,000 to 250,000 (7–18). Molecular weight distribution studies have been carried out by fractional precipitation with ethanol or 2-propanol and by complexing with anionic detergent molecules. The coacervates are isolated and recovered as gelatin fractions (19–22).

Analysis shows the presence of amino acids from 0.2% tyrosine to 30.5% glycine. The five most common amino acids are glycine [56-40-6], 26.4–30.5%;

proline [147-85-3], 14.8(18%; hydroxyproline [51-35-4], 13.3–14.5%; glutamic acid [56-86-0], 11.1–11.7%; and alanine [56-41-7], 8.6–11.3%. The remaining amino acids in decreasing order are arginine [74-79-3], aspartic acid [56-84-8], lysine [56-87-1], serine [56-45-1], leucine [61-90-5], valine [72-18-4], phenylalanine [63-91-2], threonine [72-19-5], isoleucine [73-32-5], hydroxylysine [13204-98-3], histidine [71-00-1], methionine [63-68-3], and tyrosine [60-18-4] (18–25).

Warm gelatin solutions are more levorotatory than expected on the basis of the amino acid composition, indicating additional order in the molecule, which probably results from Gly-Pro-Pro and Gly-Pro-Hypro sequences (26). The α-chain form of gelatin behaves in solution like a random-coil polymer, whereas the gel form may contain as much as 70% helical conformation (27). The remaining molecules in nonhelical conformation link helical regions together to form the gel matrix. Helical regions are thought to contain both inter- and intramolecular associations of chain segments.

Gelatin structures have been studied with the aid of an electron microscope (28). The structure of the gel is a combination of fine and coarse interchain networks; the ratio depends on the temperature during the polymer–polymer and polymer–solvent interaction leading to bond formation. The rigidity of the gel is approximately proportional to the square of the gelatin concentration. Crystallites, indicated by X-ray diffraction pattern, are believed to be at the junctions of the polypeptide chains (29).

Homogeneous α-chain gelatin has been prepared by pretreating collagen with pronase in the presence of 0.4 *M* CaC_{l2} [10043-52-4], and extracting the gelatin with hot water at 80°C and pH 7.0 after inactivating the enzyme and removing the salts.

2.1. Stability. Dry gelatin stored in airtight containers at room temperature has a shelf life of many years. However, it decomposes above 100°C. For complete combustion, temperatures above 500°C are required. When dry gelatin is heated in air at relatively high humidity, <60% rh, and at moderate temperatures, ie, above 45°C, it gradually loses its ability to swell and dissolve (25,26). Aqueous solutions or gels of gelatin are highly susceptible to microbial growth and breakdown by proteolytic enzymes. Stability is a function of pH and electrolytes and decreases with increasing temperature because of hydrolysis.

3. Physical and Chemical Properties

Commercial gelatin is produced in mesh sizes ranging from coarse granules to fine powder. In Europe, gelatin is also produced in thin sheets for use in cooking. It is a vitreous, brittle solid, faintly yellow in color. Dry commercial gelatin contains about 9–13% moisture and is essentially tasteless and odorless with specific gravity between 1.3 and 1.4. Most physical and chemical properties of gelatin are measured on aqueous solutions and are functions of the source of collagen, method of manufacture, conditions during extraction and concentration, thermal history, pH, and chemical nature of impurities or additives.

3.1. Gelation. Perhaps the most useful property of gelatin solution is its capability to form heat reversible gel–sols. When an aqueous solution of gelatin with a concentration greater than about 0.5% is cooled to about 35–40°C, it first

increases in viscosity, and then forms a gel. The gelation process is thought to proceed through three stages: (*1*) rearrangement of individual molecular chains into ordered, helical arrangement, or collagen fold (27–39); (*2*) association of two or three ordered segments to create crystallites (34,40,41); and (*3*) stabilization of the structure by lateral interchain hydrogen bonding within the helical regions. The rigidity or jelly strength of the gel depends on the concentration, the intrinsic strength of the gelatin sample, pH, temperature, and additives.

Because the economic value of gelatin is commonly determined by jelly strength, the test procedure for its determination is of great importance. Commercially, gelatin jelly strength is determined by standard tests which measure the force required to depress the surface of a carefully prepared gel by a distance of 4 mm using a flat-bottomed plunger 12.7 mm in diameter. The force applied may be measured in the form of the quantity of fine lead shot required to depress the plunger and is recorded in grams. The measurement is termed the Bloom strength after the inventor of the lead shot device (42,43). In the early 1990s, sophisticated testing equipment utilizing sensitive load cells for the measurement are commonly used.

The conversion temperature for gelatin is determined as setting point, ie, sol to gel, or melting point, ie, gel to sol. Commercial gelatins melt between 23 and 30°C, with the setting point being lower by 2–5°C. Melting point determination, described in Reference 44, utilizes test tubes filled with gelatin solution that are gently chilled to form a gel. The tubes are tilted and colored carbon tetrachloride solution is placed on the gelatin surface. The tube is gradually warmed and the end point is determined when the descent of the colored solution is observed. Several methods have been used to determine the setting point of gelatin (45).

3.2. Solubility. In most commercial applications, gelatin is used as a solution. Gelatin is soluble in water and in aqueous solutions of polyhydric alcohols such as glycerol [56-81-5] and propylene glycol [57-55-6]. Examples of highly polar, hydrogen-bonding organic solvents in which gelatin dissolves are acetic acid [64-19-7], trifluoroethanol [75-89-8], and formamide [75-12-7] (46). Gelatin is practically insoluble in less polar organic solvents such as acetone, carbon tetrachloride, ethanol, ether, benzene, dimethylformamide, and most other nonpolar organic solvents. Many water-soluble organic solvents are compatible with gelatin, but interfere with gelling properties (47). Dry gelatin absorbs water exothermally. The rate and degree of swelling is a characteristic of the particular gelatin. Swelled gelatin granules dissolve rapidly in water above 35°C. The crosslinking of gelatin matrix by chemical means is used extensively in photographic products, and this so-called hardening permanently reduces the solubility of gelatin (33,48–54).

3.3. Amphoteric Character. The amphoteric character of gelatin is due to the functional groups of the amino acids and the terminal amino and carboxyl groups created during hydrolysis. In strongly acidic solution the gelatin is positively charged and migrates as a cation in an electric field. In strongly alkaline solution, it is negatively charged and migrates as an anion. The intermediate point, where net charge is zero and no migration occurs, is known as the isoelectric point and is designated in pH units (55,56). A related property, the isoionic point, can be determined by utilizing a mixed-bed ion-exchange resin to remove

all nongelatin cations and anions. The resulting pH of the gelatin solution is the isoionic point and is expressed in pH units. The isoionic point is reproducible, whereas the isoelectric point depends on the salts present. Type A gelatin has a broad isoionic region between pH 7 and pH 10; type B is in a lower, more reproducible region, reaching an isoionic point of 5.2 after 4 weeks of liming, which drops to 4.8 after prolonged or more vigorous liming processes (57–60). The isoelectric point can also be estimated by determining a pH value at which a gelatin solution exhibits maximum turbidity (61). Many isoionic point references are recorded as isoelectric points even though the latter is defined as a pH at which gelatin has net charge of zero and thus shows no movement in the electric field (62).

3.4. Viscosity. The viscosity of gelatin solutions is affected by gelatin concentration, temperature, molecular weight of the gelatin sample, pH, additives, and impurities. In aqueous solution above 40°C, gelatin exhibits Newtonian behavior. Standard testing methods employ use of a capillary viscometer at 60°C and gelatin solutions at 6.67 or 12.5% solids (43,45). The viscosity of gelatin solutions increases with increasing gelatin concentration and with decreasing temperature. For a given gelatin, viscosity is at a minimum at the isoionic point and reaches maxima at pH values near 3 and 10.5 (63). At temperatures between 30 and 40°C, non-Newtonian behavior is observed, probably due to linking together of gelatin molecules to form aggregates (64,65). Addition of salts decreases the viscosity of gelatin solutions. This effect is most evident for concentrated gelatin solutions (66–68).

3.5. Colloid and Emulsifying Properties. Gelatin is an effective protective colloid that can prevent crystal, or particle, aggregation, thereby stabilizing a heterogeneous suspension. It acts as an emulsifying agent in cosmetics and pharmaceuticals involving oil-in-water dispersions. The anionic or cationic behavior of gelatin is important when used in conjunction with other ionic materials. The protective colloid property is important in photographic applications where it stabilizes and protects silver halide crystals while still allowing for their normal growth and sensitization during physical and chemical ripening processes.

Coacervation. A phenomenon associated with colloids wherein dispersed particles separate from solution to form a second liquid phase is termed *coacervation*. Gelatin solutions form coacervates with the addition of salt such as sodium sulfate [7757-82-6], especially at pH below the isoionic point. In addition, gelatin solutions coacervate with solutions of oppositely charged polymers or macromolecules such as acacia. This property is useful for microencapsulation and photographic applications (69–74).

Swelling. The swelling property of gelatin is not only important in its solvation but also in photographic film processing and the dissolution of pharmaceutical capsules. That pH and electrolyte content affect swelling has been explained by the simple Donnan equilibrium theory, treating gelatin as a semipermeable membrane (75). This explains why gelatin exhibits the lowest swelling at its isoelectric pH. At pH below the isoelectric point, proper choice of anions can control swelling, whereas above the isoelectric point, cations primarily affect swelling. These effects probably involve breaking hydrogen bonds, resulting in increased swelling. The rate of swelling follows approximately a second-order

equation (76,77). In photographic products, the swelling of the gelatin layer is controlled by coating conditions, drying conditions, chemical cross-linking, and the composition of the processing solutions (49–54). Conditioning at 90% rh and 20°C for 24 h greatly reduces swelling of hot dried film coatings (78–80). The ratio of lateral to vertical swelling is of great concern in the photographic industry since it can cause curling of photographic papers or films when changes in humidity or general moisture content take place.

4. Manufacture and Processing

Although new methods for processing gelatin, including ion exchange and cross-flow membrane filtration, have been introduced since 1960, the basic technology for modern gelatin manufacture was developed in the early 1920s. Acid and lime processes have separate facilities and are not interchangeable. In the past, bones and ossein, ie, decalcified bone, have been supplied by India and South America. In the 1990s, slaughterhouses and meat-packing houses are an important source of bones. The supply of bones has been greatly increased since the meat-packing industry introduced packaged and fabricated meats, assisted by the growth of fast-food restaurants. Dried and rendered bones yield about 14–18% gelatin, whereas pork skins yield about 18–22%.

Most type A gelatin is made from pork skins, yielding grease as a marketable by-product. The process includes macerating of skins, washing to remove extraneous matter, and swelling for 10–30 h in 1–5% hydrochloric acid [7647-01-0], phosphoric acid [7664-38-2], or sulfuric acid [7664-93-9]. Then four to five extractions are made at temperatures increasing from 55–65°C for the first extract to 95–100°C for the last extract. Each extraction lasts about 4–8 h. Grease is then removed, the gelatin solution filtered, and, for most applications, deionized. Concentration to 20–40% solids is carried out in several stages by continuous vacuum evaporation. The viscous solution is chilled, extruded into thin noodles, and dried at 30–60°C on a continuous wire-mesh belt. Drying is completed by passing the noodles through zones of successive temperature changes wherein conditioned air blows across the surface and through the noodle mass. The dry gelatin is then ground and blended to specification.

Type B gelatin is made mostly from bones, but also from bovine hides and pork skins. The bones for type B gelatin are crushed and degreased at the rendering facilities, which are usually located at a meat-packing plant. Rendered bone pieces, 0.5–4 cm, with less than 3% fat, are treated with cool, 4–7% hydrochloric acid from 4 to 14 days to remove the mineral content. An important by-product, dibasic calcium phosphate, is precipitated and recovered from the spent liquor. The demineralized bones, ie, ossein, are washed and transferred to large tanks where they are stored in a lime slurry with gentle daily agitation for 3–16 weeks. During the liming process, some deamination of the collagen occurs with evolution of ammonia. This is the primary process that results in low isoelectric ranges for type B gelatin. After washing for 15–30 h to remove the lime, the ossein is acidified to pH 5–7 with an appropriate acid. Then the extraction processing for type A gelatin is followed. Throughout the manufacturing process, cleanliness is important to avoid contamination by bacteria or proteolytic enzymes.

Bovine hides and skins are substantial sources of raw material for type B gelatin and are supplied in the form of splits, trimmings of dehaired hide, rawhide pieces, or salted hide pieces. Like pork skins, the hides are cut to smaller pieces before being processed. Sometimes the term calfskin gelatin is used to describe hide gelatin. The liming of hides usually takes a little longer than the liming of ossein from bone.

Most manufacturing equipment should be made of stainless steel. The liming tanks, however, can be either concrete or wood. Properly lined iron tanks are often used for the washing and acidification, ie, souring, operations. Most gelatin plants achieve efficient processes by operating around the clock. The product is tested in batches and again as blends to confirm conformance to customer specifications.

5. Economic Aspects

World gelatin production in 2000 was believed to be about 260,000 t. The United States produced about 45,000 t, followed by Germany, France, Brazil, Japan, and India. Of the gelatin produced in the United States, 59% is acid-processed, ie, type A. The U.S. food industry consumes about 25,000 t/year, with an annual growth rate of 0.5%; the pharmaceutical industry consumes about 20,000 t/year; and the photographic industry about 10,000 t/year. In the United States, the pharmaceutical gelatin market is expected to grow on the average of 2.5% per year. The photographic gelatin market has been stable or declining slightly.

6. Analytical Test Methods and Quality Standards

Gelatin is identified by a positive test for hydroxyproline [51-35-4], turbidity with tannic acid [1401-55-4], or a yellow precipitate with acidic potassium dichromate [7778-50-9] or trinitrophenol [88-89-1]. A 5% aqueous solution exhibits reversible gel-to-sol formation between 10 and 60°C. Gelatin gives a positive color test for aldehydes and sugars that are considered undesirable impurities in photographic gelatin; nucleic acids are considered restrainers in photographic gelatins and their concentration is monitored closely for this application (81). Elemental analysis of commercial gelatin is reported as carbon, 50.5%; hydrogen, 6.8%; nitrogen, 17%; and oxygen 25.2% (82); a purer sample analyzed for 18.2–18.4% nitrogen (23,25). Regulations for quality standards vary from country to country, but generally include specifications for ash content, SO_2, heavy metals, chromium, lead, fluoride, arsenic, odor, and for the color or clarity of solutions (83). In addition, certain bacteriological standards, including E. coli and Salmonella, are specified. Restrictions on certain additives and preservatives are also listed. In the United States, the *Food Chemicals Codex* published an updated specification for food-grade gelatin in 1996. Standard testing procedures for viscosity, pH, ash, moisture, heavy metals, arsenic, bacteria, and jelly strength are described (42,83–87). Additional test procedures have been published by the photographic and gelatin industries including the Japanese PAGI Method (88,89). Specific tests for photographic gelatin have been devised by the

International Working Group for Photographic Gelatin (IAG) (90) in Fribourg, Switzerland, and by individual photographic companies and gelatin companies.

7. Uses

7.1. Food Products. Gelatin formulations in the food industry use almost exclusively water or aqueous polyhydric alcohols as solvents for candy, marshmallow, or dessert preparations. In dairy products and frozen foods, gelatin's protective colloid property prevents crystallization of ice and sugar. Gelatin products having a wide range of Bloom and viscosity values are utilized in the manufacture of food products, specific properties being selected depending on the needs of the application. For example, a 250-Bloom gelatin may be utilized at concentrations ranging from 0.25% in frozen pies to 0.5% in ice cream; the use of gelatin in ice cream has greatly diminished. In sour cream and cottage cheese, gelatin inhibits water separation, ie, syneresis. Marshmallows contain as much as 1.5% gelatin to restrain the crystallization of sugar, thereby keeping the marshmallows soft and plastic; gelatin also increases viscosity and stabilizes the foam in the manufacturing process. Many lozenges, wafers, and candy coatings contain up to 1% gelatin. In these instances, gelatin decreases the dissolution rate. In meat products, such as canned hams, various luncheon meats, corned beef, chicken rolls, jellied beef, and other similar products, gelatin in 1–5% concentration helps to retain the natural juices and enhance texture and flavor. Use of gelatin to form soft, chewy candies, so-called gummi candies, has increased worldwide gelatin demand significantly (ca 1992). Gelatin has also found new uses as an emulsifier and extender in the production of reduced-fat margarine products. The largest use of edible gelatin in the United States, however, is in the preparation of gelatin desserts in 1.5–2.5% concentrations. For this use, gelatin is sold either premixed with sugar and flavorings or as unflavored gelatin packets. Most edible gelatin is type A, but type B is also used.

7.2. Pharmaceutical Products. Gelatin is used in the pharmaceutical industry for the manufacture of soft and hard capsules. The formulations are made with water or aqueous polyhydric alcohols. Capsules are usually preferred over tablets in administering medicine (91). Elastic or soft capsules are made with a rotary die from two plasticized gelatin sheets which form a sealed capsule around the material being encapsulated. Methods have been developed to encapsulate dry powders and water-soluble materials which may first be mixed with oil. The gelatin for soft capsules is low bloom type A, 170–180 g; type B, 150–175 g; or a mixture of type A and B. Hard capsules consisting of two parts are first formed and then filled. The manufacturing process is highly mechanized and sophisticated in order to produce capsules of uniform capacity and thickness. Medium-to-high bloom type A, 250–280 g; type B, 225–250 g; or the combination of type A and B gelatin are used for hard capsules. Usage of gelatin as a coating for tablets has increased dramatically. In a process similar to formation of gelatin capsules, tablets are coated by dipping in colored gelatin solutions, thereby giving the appearance and appeal of a capsule, but with some protection from

adulteration of the medication. The use of glycerinated gelatin (83) as a base for suppositories offers advantages over carbowax or cocoa butter base (92). Coated or cross-linked gelatin is used for enteric capsules. Gelatin is used as a carrier or binder in tablets, pastilles, and troches.

For arresting hemorrhage during surgery, a special sterile gelatin sponge known as absorbable gelatin sponge (28) or Gelfoam is used. The gelatin is partially insolubilized by a cross-linking process. When moistened with a thrombin or sterile physiological salt solution, the gelatin sponge, left in place after bleeding stops, is slowly dissolved by tissue enzymes. Special fractionated and prepared type B gelatin can be used as a plasma expander.

Gelatin can be a source of essential amino acids when used as a diet supplement and therapeutic agent. As such, it has been widely used in muscular disorders, peptic ulcers, and infant feeding, and to spur nail growth. Gelatin is not a complete protein for mammalian nutrition, however, since it is lacking in the essential amino acid tryptophan [73-22-3] and is deficient in sulfur-containing amino acids.

7.3. Photographic Products. Gelatin has been used for over 100 years as a binder in light-sensitive products. The useful functions of gelatin in photographic film manufacture are a result of its protective colloidal properties during the precipitation and chemical ripening of silver halide crystals, setting and film-forming properties during coating, and swelling properties during processing of exposed film or paper. Quality requirements of photographic gelatin may be very elaborate and can include over 40 chemical and physical tests, in addition to photographic evaluation. Most chemical impurities are limited to less than 10 ppm. Aqueous solutions are employed for emulsions. Photographic gelatins are manufactured to standard specifications since the testing is time-consuming and costly. A new gelatin product may require 6–12 months of testing, including extensive field testing prior to commercialization. Photographic products may have up to 20 gelatin layers grouped into three categories: (*1*) light-sensitive silver halide-bearing layers of 2–10 μm thickness, referred to as emulsion layers; (*2*) surface, spacer, filter, or protective layers of 1–2 μm thickness; and (*3*) backing, antihalo, or noncurl layers coated on the opposite side of the film substrate from the emulsion layer. The quality and uniformity standards are highest for emulsion gelatin because it controls silver halide nucleation, crystal growth, chemical sensitization, latent image stability, and numerous other factors affecting the total photographic response. Since the early 1970s, the photographic industry has switched from so-called active gelatins derived from hides to inert types derived from bones. The latter are very low or void of natural restrainers, reduction, and sulfur sensitizers. Other changes in techniques have been brought about by abandoning the lengthy noodle wash technique used to remove salts after silver halide precipitation in favor of precipitating, coagulating, or derivatizing gelatin and washing the precipitate by decanting or utilizing ultrafiltration techniques; by new coating techniques that allow simultaneous coating of several layers at one time at speeds 10 times as fast as before; and by short-time high temperature processing which may require new cross-linking agents unlike the aldehydes and metal salts previously used. Many new hardeners are extremely fast-acting and are metered into the solution during the coating operation. It is quite common to use a derivatized gelatin, such as phthalated

gelatin, to precipitate silver halide (74). These materials with a low pH isoionic point form a coacervate at pH < 4.0. Precipitation in this case is accomplished by lowering the pH, washing at low pH, and then increasing pH to above 6.5 to dissolve and redisperse the emulsion before reconstituting it with gelatin. Gelatin used in the auxiliary layers must be able to withstand high temperature processing and allow high speed coating.

Gelatin is also used in so-called subbing formulations to prepare film bases such as polyester, cellulose acetate [9004-35-7], cellulose butyrate, and polyethylene-coated paper base for coating by aqueous formulations. Solvents such as methanol [67-56-1], acetone [67-64-1], or chlorinated solvents are used with small amounts of water. Gelatin containing low ash, low grease, and having good solubility in mixed solvents is required for these applications (see Coatings). In certain lithographic printing, light-sensitive dichromated gelatin is used. Light causes permanent cross-linking of gelatin in the presence of the dichromate; this phenomenon is used to make relief images for printing. Dichromated gelatin coatings are commonly used in production of high quality holographic images. In this application, the light sensitivity of the image-receiving medium is less important than the image-resolving power (93,94). Gelatin coatings in photographic products are further tested for brittleness, scratch resistance, friction, swelling rate, drying rate, curling tendency, dry adhesion, wet adhesion, and pressure sensitivity. These properties are becoming more critical with the development of more sophisticated cameras and printing and processing equipment. Photographic technology offers a rapidly changing, highly sophisticated, very competitive market for photographic gelatin manufacturers.

7.4. Derivatized Gelatin. Chemically active groups in gelatin molecules are either the chain terminal groups or side-chain groups. In the process of modifying gelatin properties, some groups can be removed, eg, deamination of amino groups by nitrous acid [10024-97-2] (95), or removal of guanidine groups from arginine [74-79-3] by hypobromite oxidation (96); the latter destroys the protective colloid properties of gelatin. Commercially successful derivatized gelatins are made mostly for the photographic gelatin and microencapsulation markets. In both instances, the amino groups are acylated. Protein detergent is made by lauroylating gelatin. Phthalated gelatin is now widely used in the photographic industry (97). Arylsulfonylated gelatin has been patented for microencapsulation (98). Carbamoylated gelatin, made by treating gelatin with cyanate or nitrourea in neutral aqueous solution, is also used by the photographic industry (24,99–101). Active double bonds react with the amino groups in gelatin, and acrylic polymers have been grafted to gelatin (102). Gelatin has been derivatized by epoxides (103), cyclic sulfones (104), and cyanamide [420-04-2] (105). Cross-linking or hardening of gelatin attacks the same active groups, but an agent with two active sites is needed, eg, divinylsulfone [77-77-0], bis(isomaleimide) [13676-54-5], aziridines, bisepoxides, epichlorohydrin [106-89-8], polyisocyanates, and dichlorotriazine. Aldehydes such as formaldehyde [50-00-0] and glyoxal [107-22-2] are still used and to a small extent even potassium chromium alum [7788-99-0], $Cr_2K_2(SO_4)_4 \cdot 24\ H_2O$, and potassium aluminum alum [7784-24-9], $Al_2K_2(SO_4)_4 \cdot 24\ H_2O$.

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