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Biodegradable Polymers and their Applications in Drug Delivery System

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Abstract

Biodegradable polymers have proved to be useful in versatile applications, including controlled drug delivery, gene delivery, regenerative medicine, and other biomedical applications. Their desirable characteristic features of ample abundance, biocompatibility, and biodegradability make them potential for various uses. Biodegradable polymers are again classified into proteins and polysaccharides. Proteins include Bovine serum albumin, gelatin, lectin, legumin and polysaccharides include chitosan, sodium alginate, dextran, agarose, pollulan and carbapol. The synthetic polymers that can be used are Poly lactic acid (PLA), Ethyl cellulose, Eudragit® S100, Poly lactide coglycolides (PLGA), Poly epsilon caprolactone, Poly ethylene glycol (PEG) and so forth. Biodegradable natural polymers are derived from renewable resources, which mean for example plants, animals and microorganisms, and thus they usually have an excellent biocompatibility and are naturally biodegradable.

Keywords: Bovine Serum Albumin; Gelatin; Bioegradable Polymers; Drug Delivery.

Introduction

Proteins are essentially high-molecular-weight polymers composed of amino acid monomers joined by amide bonds. They often occur in 3D folded structures and are one of the most common materials found in the human body. Proteins polymers have been utilized as biomaterials in sutures, scaffolds, and drug delivery devices [1, 2].

Proteins have an important role in both biological and material fields. These are biodegradable and non-antigenic. Proteins are thermoplastic heteropolymers. They are constituted by both different polar and non-polar α-aminoacids. Aminoacids are able to form a lot of intermolecular linkages resulting in different interactions [3, 4].

Bovine Serum Albumin

Introduction

Bovine serum albumin (also known as BSA or "Fraction V") is a serum albumin protein derived from cows. It is often used as a protein concentration standard. BSA is also called as "Fraction V". It refers to albumin being the fifth fraction of the original Edwin Cohn purification methodology that made use of differential solubility characteristics of plasma proteins. The process was first commercialized with human albumin for medical use and later adopted for production of BSA.

Bovine serum albumin (BSA) is a large globular protein with a good essential amino acid profile. It has been well characterized and the physical properties are well known by peters in 1975. Bovine Serum Albumin (BSA) is a macromolecular carrier and is widely used to prepare nanoparticles, due to its biodegradability, non toxicity and non immunogenicity. BSA can be considered as an attractive polymer that can be used as a good carrier for drugs. On the other hand, albumin nanoparticles are biodegradable, easy to prepare in defined sizes, and carry drug entities on their surfaces by covalent linkage that can be used for ligand binding. BSA are rich in charged amino acids (lysine) that allow the positive and negative charged molecules to adsorb electro statically without the participation of any other compounds. BSA nanoparticles are nontoxic, biodegradable and biocompatible material, which are easily adaptable to the human body. It has potential usefulness in transporting fatty acids, endogenous and exogenous compounds throughout the body.

Bovine serum albumin (BSA) binds free fatty acids, other and flavor compounds which can alter the heat denaturation of the protein. Isolated BSA has been reported to be very drug & polymer profile. It is reported to particularly unfold between 40 and 50°C, exposing non-polar residues on the surface and facilitating reversible protein-protein interactions. Phospholipid-protein-calcium complexes are formed at pH levels below the iso-electric point of the BSA [5, 6].

Bovine Serum Albumin is an abundant water-soluble blood protein comprising almost 50% of total plasma mass in the body.

Albumin carries hydrophobic fatty acids in the blood stream as well as carefully maintains blood pH. As Albumin is essentially ubiquitous in the body, nearly all tissues have enzymes that can degrade it making it a promising polymer for biomedical applications. Because of its serological compatibility and weak mechanical strength, albumin has been primarily investigated for payload delivery, coating, and suturing applications.

Structure of Bovine serum albumin

BSA is a single polypeptide chain consisting of about 583 amino acid residues and no carbohydrates. Non-glycoprotein, cross-linked with 17 cysteine residues. The full-length BSA precursor protein is 607 amino acids (AAs) in length. An N-terminal 18-residue signal peptide is cut off from the precursor protein upon secretion; hence the initial protein product contains 589 amino acid residues. An additional six amino acids are cleaved to yield the BSA protein that contains 583 amino acids. Three types of intrinsic fluorophores are present in BSA: tryptophan (Trp), tyrosine (Tyr) and phenylalanine (Phe). There are two tryptophan residues in BSA, Trp-212 is located in a hydrophobic binding pocket and Trp-134 on the surface of molecule. The BSA molecule is made up of three homologous domains (I, II, III) that can be divided into nine loops (L1–L9) by 17 disulphide bonds. Each domain in turn is the product of two subdomains (IA, IB, etc.). Trp-134 is in the first domain, and Trp-212 is in the second domain. At pH 5-7 it contains 17 intra chain disulfide bridges and 1 sulfhydryl group. All these structural features make BSA one of the best models to understand the physicochemical basis of polymer-protein interactions. A pictorial representation of the BSA model structure obtained from homology modelling indicating the domains and the binding sites [7, 8]. (e.g., see Figure 1).

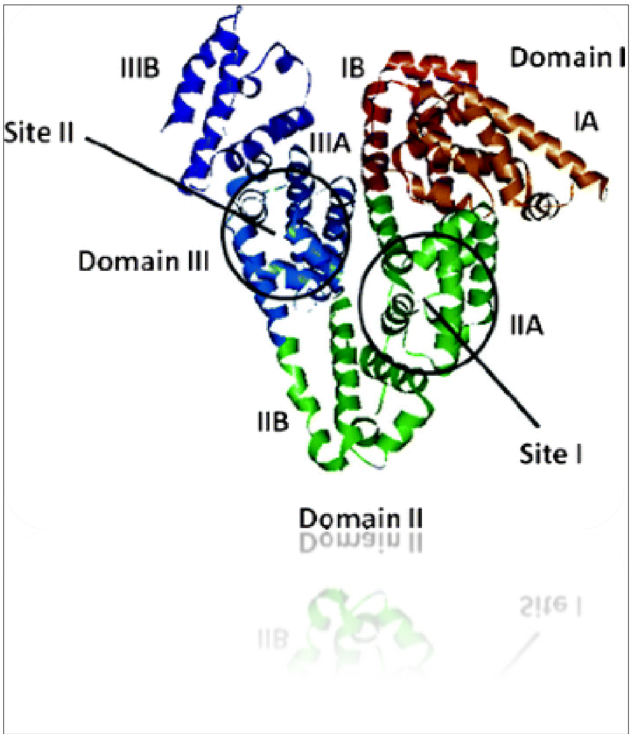

Figure 1: BSA Model Structure (From Satyajit Patra et al, RSC Advances, 2, 6079-6086, 2012)

Physiochemical Properties

Color	: White or yellow appearance
Solubility	: Soluble in water
Molecular weight	: 66,463 Da (= 66.5 kDa)
Storage temperature	: 2-8°C
Number of amino Acid residues	: 583
Isometric point in water	: 25°C: 4.7
pH of 1% Solution	: 5.2-7
Optical Rotation	: $[\alpha]_{259}$: -61°; $[\alpha]_{264}$: -63°
Diffusion constant $D_{20,W} \times 10^{-7}$ cm^2/s	: 5.9
Partial specific volume, V_{20}	: 0.733
Intrinsic viscosity, η	: 0.0413
Frictional ratio, f/f0	: 1.30
Stokes Radius (r_s)	: 3.48 nm
Mean residue rotation, $[m']_{233}$	: 8443
Mean residue ellipticity	: 21.1 $[\theta]_{209\ nm}$; 20.1 $[\theta]_{222\ nm}$
Estimated a-helix, %	: 54
Estimated b-form, %	: 18
Sedimentation constant, S_{20},W × 10^{13}	: 4.5 (monomer), 6.7 (dimer)
The solution stability	:Is very good

Method of Preparation

HISTORY: Albumin is relatively simple to isolate and purify. One of the first methods of isolation involved extensive dialysis of serum against water; this process removed most globulins. A second procedure took advantage of the good solubility of albumin at low to moderate ammonium sulfate concentrations, and effected precipitation by lowering the pH. Electrophoretic isolation was also employed, as was affinity chromatography. None of these methods were applicable to large scale production [9].

INITIAL ISOLATION: Initial isolation is by Heat Treatment or by Alcohol precipitation. Most commercial preparations are now prepared by Alcohol Precipitation, A method developed by E. J. Cohn and his associates in the 1940's ("Fraction V" yields albumin with a purity of about 96%) or by Heat Treatment.

FURTHER PURIFICATION: Additional removal of impurities can be accomplished by crystallization. preparative electrophoresis, ion exchange chromatography, affinity chromatography (e.g., ConA-agarose removes glycoproteins), heat treatment (removes globulins), low pH treatment, charcoal treatment, and low temperature treatment. Charcoal treatment and organic solvent precipitation remove fatty acids [10].

Advantages

BSA exhibits many advantages due to its good stability and better sustained release properties. The advantages of BSA are as follows:

- Biodegradable
- Biocompatible
- Eco-friendly
- Inexpensive
- BSA is easily adaptable to the human body.
- BSA has potential usefulness in transporting fatty acids, endogenous and exogenous compounds throughout the body.
- Good stability
- Non-toxic
- Ready availability

Disadvantages

- Possible microbial contamination during production due to their natural sources.
- Slow process as production rate depends upon the environment and many other factors.

Applications

BSA has numerous applications

- BSA is a natural biodegradable polymer and a globular protein that is mainly used in numerous biochemical applications due to its stability and lack of interference within biological reaction.
- BSA is mainly used as a polymer in the preparation of nanoparticles.
- BSA has numerous biochemical applications including ELISAs (Enzyme-Linked Immunosorbent Assay), immunoblots, and immunohistochemistry.
- In immunohistochemistry, BSA is used to study how cancerous tumors behave and grow.
- In molecular biology, BSA is used to stabilize some restriction enzymes during digestion of DNA and to prevent adhesion of the enzyme to reaction tubes, pipette tips, and other vessels.
- BSA is considered to be a universal blocking reagent in many applications.
- BSA is also used as in cell nutrient and microbial culture.
- BSA is commonly used to determine the quantity of other proteins, by comparing an unknown quantity of protein to known amounts of BSA.
- Bovine serum albumin binds to a long chain fatty acids and makes them water soluble.
- BSA may protect mammalian cells against certain genotoxic agents.
- In cell culture, BSA is used in cell culture mediums as a supplement to feed cells and support cell growth.
- Bovine serum albumin has been primarily investigated for payload delivery, coating, and suturing applications.
- BSA is used in electrophoresis.
- BSA also used as blood banking reagent.
- BSA is general blocking reagent in ELISA, as a nutrient in cell & microbial culture, it also stabilize some enzymes during digestion of DNA.
- BSA is used in Antibody purification.
- Various endogenous and exogenous ligands are transported by BSA.
- Used in Binding and transport studies.
- BSA used as Protein base or filler, Protein supplement and Protein standard.
- Used in Serology.
- Used as Hapten carrier.
- Used in Immunohematology, Molecular biology.
- Used in Mitogenic assays.
- Also used in Enzyme systems.
- BSA is used to solubilize lipids, stabilize protein solutions.
- Currently, a bovine albumin-based adhesive marketed as BioGlue®(CryoLife) is FDA approved for vascular surgery.

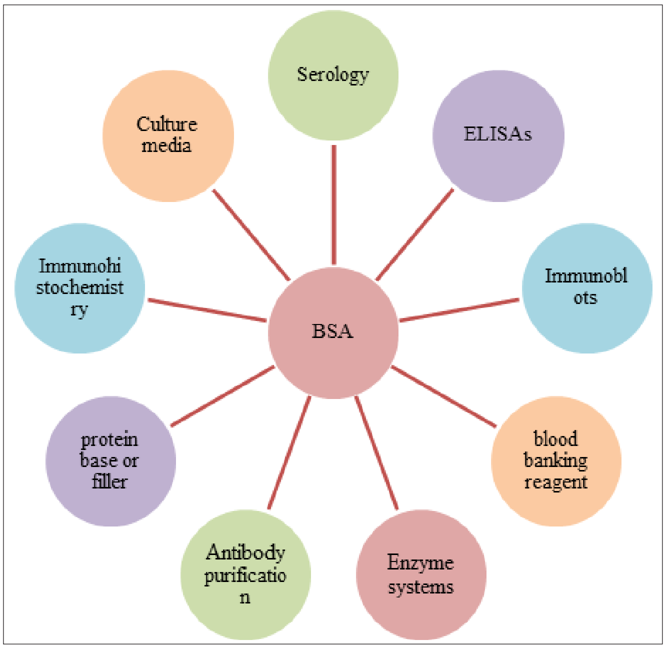

Figure 2: Applications of Bovine serum albumin.

GELATIN

Introduction

Gelatin or gelatine (derived from Latin word: gelatus meaning "stiff" or "frozen"). Gelatin is a type of protein produced by the partial hydrolysis of native collagen. Collagen recognized as a biodegradable and biocompatible starting material being in use as plasma expander for decades. Gelatin is obtained by hydrolysis of collagen which is found as the major component of skin, bones and connective tissue is one of the protein materials. The natural source of gelatin is from animals. It is obtained mainly by acidic or alkaline, but also thermal or enzymatic degradation of the collagen [11, 12].

Gelatin, one of the most versatile, naturally occurring biopolymers, is widely used in food products, pharmaceutical and medical applications.

Gelatin is a water soluble proteinaceous substance specifically by the partial hydrolysis of collagen derived from the skin, white connective tissue and bones of animals. Collagen forms 30% of all vertebrate body protein with a majority in bone and skin. More than 90% of the extra cellular protein in the tendon and bone and more than 50% protein in the skin consist of collagen. The high stability bases on the unique triple-helix structure consisting of three polypeptide α-chains. So far 27 collagen types have been isolated so far, however, collagen type I (skin, tendon, bone), type II (hyaline vessels) and type III are used for the production of gelatin only. In addition; Gelatin is a biocompatible and non-immunogenic substrate of matrix metalloproteinases (MMPs).

Types of Gelatin

Two types of gelatin can be formed: Type A and Type B.

TYPE A: (Acid hydrolysis)

- It is obtained by acidic treatment of collagen.
- Has an isoelectric point (pI) between 7.0 and 9.0.
- Type-A will be positively charged at physiological pH.
- Gelatin type-A results in slightly more viscous solutions.
- It is mainly obtained from pork skin.

TYPE B: (Alkaline hydrolysis)

- It is obtained by alkaline hydrolysis of collagen.
- Has an isoelectric point (pI) between 4.8 and 5.1.
- Type-B will possess negative charges at physiological pH.
- It has been reported that gelatin type – B shows a better biocompatibility compared to gelatin type – A.
- It mainly found in animal collagen from skins, cartilage, bones, and tendons.

Structure of Gelatin

Gelatin is the high content of the amino acids glycine, proline (mainly as hydroxyproline), alanine and 4-hydroxyl proline residues. Gelatin molecules contain repeating sequences of glycine, proline and alanine amino acid triplets, which are responsible for the triple structure of gelatin. The chemical structure of gelatin is what makes gelatin water soluble, flexible and transparent and form a positive binding action that is useful in food processing, pharmaceuticals and in photography. Figure 3 depicts the basic structure of gelatin [13].

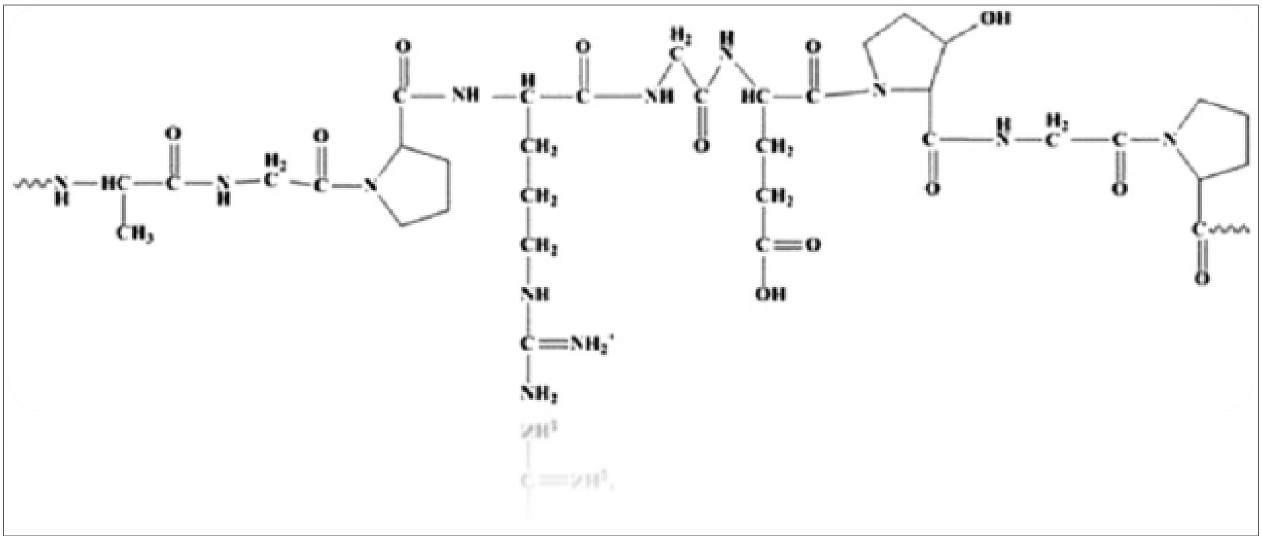

Figure 3: Structure of gelatin

Amino acid content

Gelatin is reported to contain 18 amino acids linked together in a partially ordered fashion. It is a water soluble. Tryptophane and cystine are absent, and methionine is only present at a relatively low level. Glycine is one of the three predominant amino acids in the gelatin molecule that modulate cell adhesion. The mechanical properties of these films depend on the physical and chemical characteristics of the gelatin, especially the amino acid composition and the molecular weight distribution. Combining gelatin with other biopolymers as soy protein, oils and fatty acids or certain polysaccharides may improve the physical properties of gelatin films.

Analysis shows the presence of amino acids from 0.5% tyrosine to 30.05% glycine. The five most common amino acids are glycine: 26.4%-30.5%; proline: 14.8%-18%; hydroxyproline 13.3%-14.5%; glutamic acid: 11.1%-11.7%; and alanine: 8.6%-11.3%. The remaining amino acids in decreasing order are arginine, aspartic acid, lysine, serine, leucine, valine, phenylamine, threonine, isoleucine, hydroxylysine, histidine, methionine and tyrosine. Figure 4 depicts the composition of gelatin in terms of amino acids [14].

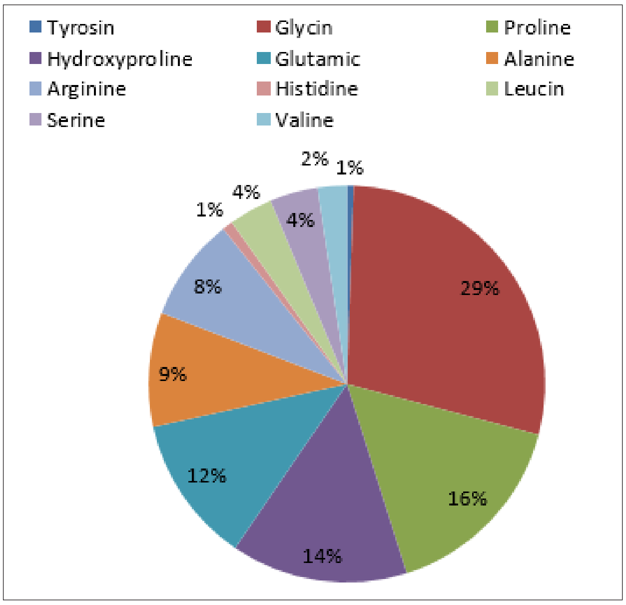

Figure 4: Amino acid composition of gelatin

Physiochemical Properties

Color : colorless

Appearance : Vitreous brittle, solid translucent and nearly tasteless powder.

Odour : Gelatin is practically odourless.

Solubility

- Soluble in water, soluble in aqueous solutions of polyhydric alcohols such as glycerol and propylene glycol.
- Insoluble in less polar organic solvents such as benzene, acetone and primary alcohols.
- Gelatin is practically insoluble in non-polar solvents such as sorbitol and mannitol.

Gel strength

- The gel strength is quoted as the bloom strength and can be defined as the weight in grams required to cause a depression of 4 mm deep to the surface of a gel by means of a piston 12.7 mm in diameter.
- The most important property of gelatin is the gel strength or "bloom", which is a function of the molecular weight of the gelatin.
- The gel strengths of gelatin typically range from 50-300 bloom.

For example Type-B gelatin with gel strengths from (125-250) is commonly used for confectionary product. Type-A gelatin with low gel strength (70-90) can be used for the fining of wine and juice.

Gelation

- It is perhaps the most useful property of gelatin solution, being the capacity to form heat reversible gel-sols. When an aqueous solution of gelatin with a concentration greater than about 0.5% is cooled to about 30-40°C, it first increases in viscosity, and then forms a gel.
- The gelation process is thought to carried out in three stages:
- Rearrangement of individual molecular chains into ordered, helical arrangement, or collagen fold.
- Association of two or three ordered segments to create crystallites.
- Stabilization of the structure by lateral interchange hydrogen bonding within the helical regions.

Molecular weight

- The weight average molecular weight of commercial gelatins may vary from about 20,000 to 250,000 Da, but very much higher molecular weights (in excess of 10^6) have been reported for gelatin fractions separated by alcohol coacervation or gel electrophoresis.
- Number average chain weights in the range 40,000 to 80,000 Da have been reported for high–grade commercial gelatins.

Viscosity

- The viscosity of gelatin solutions is affected by gelatin concentration, temperature, molecular weight of the gelatin sample, pH 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. The viscosity of gelatin solution increases with an increase in gelatin concentration and with decrease in temperature.
- For a given gelatin, viscosity is at a minimal at the isoionic point and reaches maxima at pH values near 3 and 10.5. At temperatures between 30 and 40°C, non-Newtonian behavior is observed, probably due to linking together of gelatin molecules to form aggregates.
- As addition of salts, further decreases the viscosity of gelatin solutions. This effect is most evident for concentrated gelatin solutions.

Melting point

- The melting point is the temperature at which a gelatin gel softens sufficiently, and allowing carbon tetrachloride drops to sink through it. Factors such as the mattering temperature and the concentration of the gelatin gel tends to affect its melting point.

Setting point

- The setting point of a gelatin solution is dependent on its thermal and mechanical history. Higher setting temperatures are encountered to occur, when the solution is cooled slowly in comparison to rapid chilling. Mechanical action hinders or delays setting.

Moisture Content

- Gelatin contains 8-13% of moisture content.

Relative Density : 1.3-1.4.

Swelling

- The swelling property of gelatin is not only important in its salvation but also in the dissolution of pharmaceutical capsules. This describes 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 isoelectric point, cations primarily affect swelling. These effects probably involve breaking of hydrogen bonds, results an increased swelling.
- The rate of swelling follows approximately a second – order equation. Conditioning at 90% RH and 20°C for 24 hours greatly reduces swelling of hot dried film coatings.

Storage/Stability

- Gelatin stored in air-tight containers at room temperature remains unchanged for prolonged period of time.
- When heated above 45°C in the presence of air at relatively high humidity (above 60% RH) it gradually loses its ability to swell and dissolve.
- Below 35-40°C gelatin swells in and absorbs 5-10 times its weight of water to form a gel.
- Sterile solutions of gelatin, stored cold, remain unchanged indefinitely, but at elevated temperatures hydrolysis or rupture of peptide bonds occurs, increasing the number of free amino groups.

Physicochemical properties	TYPE - A	TYPE - B
p H	3.8-5.5	5.0-7.5
Isoelectric point	7.0-9.0	4.8-5.1
Gel strength (bloom)	50-300	50-300
Viscosity (mps)	15-75	20-75
Ash %	0.3-2.0	0.5-2.0

Table 1: Physicochemical properties of Gelatin type A & B

Process of gelatin production [15]

- Although new methods for processing gelatin, including ion exchange and cross – flow membrane filtration have been introduced since 1960s, the technology for modern gelatin manufacture was developed in the early 1920s. Dried and rendered bones yield about 14-18% gelatin, whereas pork skins yield about 18-22%.
- 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 hours in 1-5% solution of hydrochloric acid, phosphoric acid, or sulfuric acid. The four to five extractions are made at temperature increasing for 55-65°C for the first extract to 95-100°C for the last extract. Each extraction lasts about 4-8 hours. Grease is removed, the gelatin solution filtered and for most applications, deionized. Concentration of 20-40% solids is carried out, in several stages by continuous vacuum evaporation. The viscous solution is chilled, extruded into thin noddles, 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 from bones, 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 hours to remove the lime, the ossein is acidified to pH 5-7 with an appropriate acid. Then the extraction process for type – A gelatin is followed. Throughout the manufacturing process, cleanliness is important to avoid contamination by bacteria or proleolytic 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, raw hide pieces or salted hide pieces. Like pork skins, the hides are cut to smaller pieces before being processed .Sometimes the term calf skin gelatin is used to describe hide gelatin, the liming of hides usually takes a little longer than the liming of ossein from bone.

Advantages

- Gelatin is a natural biopolymer with desirable properties such as:
- Good biocompatibility and biodegradability
- Water solubility
- Non-antigenicity
- Non–toxic
- Plasticity

- Adhesiveness
- Promotion of cell adhesion, growth
- Low cost
- Easy availability
- Easy to crosslink and to modify chemically
- Gelatin has been exploited as a drug carrier agent, owing to its unique chemical and physical nature.
- Gelatin has good film forming abilities.

Disadvantages

- Possible microbial contamination during production due to presence of natural sources.
- Gelatin degrades as a colloidal solution at or above 37°C, and gels at room temperature and lower.

Applications [14]

- Gelatin, is one of the most versatile, naturally occurring biopolymers, is widely used in food products and pharmaceutical formulations, photographic and other technical products.
- Gelatin is commonly used for pharmaceutical and medical applications because of its enzymatic biodegradability and biocompatibility in physiological environments.

General applications of gelatin

- Gelatin is used as a stabiliser (yoghurt), thickener (jam), and emulsifier (oil-in-water emulsions).
- Gelatin is used as a emulsifying, foaming, and wetting agent in food, pharmaceutical, medical, and technical applications due to its surface-active properties.
- Gelatin was among the first commercial raw materials suitable as a contact preservative for meat and meat products.
- It is used as a matrix for implants, in device coatings, and as a stabilizer in vaccines against measles, mumps, rubella, Japanese encephalitis, rabies, diphtheria, and tetanus toxin.
- Gelatin is also used in cosmetic industries.
- Gelatin is very useful in tissue engineering applications.
- **Industrial applications of gelatin:** Gelatin is an important hydrocolloid in the food, pharmaceutical and photographic industries.

Gelatin in food industry

- Gelatin has been widely used in food additives and healthy food due to its high content of protein and amino acid.
- The unique hydrocolloidal nature of gelatin has enabled it to find numerous applications in the food industry. These can be divided into four main groups namely; confectionery (mainly for providing chewiness, texture, and foam stabilization) and jelly deserts (to provide creaminess, fat reduction, and mouth feel), dairy products (to provide stabilization and texturization), meat products (to provide water-binding), and hydrolyzed gelatin applications.
- Gelatin is used in foods as a beverage and juice clarifier, desserts and yogurt thickener. Further uses include fruit toppings for pastry, cream cheese, and cottage cheese, as well as in food foams and fruit salads.
- Gelatin is also used in coating meat products to reduce color deterioration. Gelatin is used in canned meat products such as hams, Vienna sausages, and cured, canned pork, to hold juices lost during cooking and to provide a good heat transfer medium during cooking.
- Gelatin is also used in emulsified meats and jellied products at levels ranging from 3 to 15%, but more typically from 0.5 to 3%.
- Many lozenges, wafers and candy coatings contain up to 1% gelatin.
- Gelatin has also found as an emulsifier and extender in the production of reduced fat margarine products. A variety of examples are given in Table 2

FUNCTION	USES
Whipping agent	Marshmallows, nougats, mousses, chiffons, whipped cream.
Protective colloid	Confectionery, icings, ice creams, frozen desserts and confections.
Binding agent	Meat rolls, canned meats, confectionery, cheeses, dairy products.
Film former	Coating for fruits, meat items.
Thickener	Powdered drink mixes, gravies, sauces, soups, puddings, jellies, syrups, dairy products
Emulsifier	Cream soups, sauces, flavorings, meat pastes, whipped cream, confectionery, dairy products.

Table 2: Functional properties of gelatin in foods

Source: Abdalbasit Adam et al. REVIEW: Gelatin, Source, Extraction And Industrial Applications, Acta Scientiarum Polonorum Technologia Alimentaria. ACTA, 2013, 12(2),pp 135-147.

Gelatin in pharmaceutical applications:

- The largest proportion of gelatin procured by the pharmaceutical industry is mainly used for hard and soft gelatin capsules (Softgels) and for tableting, tablet coating, tablet binder, granulation, encapsulation and microencapsulation. Where it helps prevent oxidation and makes the preparation more palatable. Also used in suppositories.
- Coated or cross – linked gelatin is used for enteric capsules.
- Gelatin is used as a carrier or binder in tablets, pastilles and troches.

- Gelatins with bloom in the range of 0 to 140 are offered for the microencapsulation of vitamins A, D and E. Fish gelatins have exceptionally good film forming properties and are offered for microencapsulation.
- Gelatin can be a source of essential amino acids when used as a diet supplement . As it has been widely used in muscular disorders, peptic ulcers, and infant feeding and to spur nail growth.
- Gelatin capsule formulations contain a wide variety of other ingredients. Gelatin capsules (gel-caps) are commonly used to encapsulate nutritional supplements, and medicines.
- The gelatin for soft capsules is low bloom type – A 170-180 g; type − B 150-175g; or a mixture of type – A and type – B. 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.
- Gelatin is used as excipient in pharmaceutical preparations, including vaccines, and is used as a binder for tablets, excipients may be originating from quite distinct sources, including gelatin.
- In surgery for arresting hemorrhage, a special sterile gelatin sponge knows as absorbable gelatin sponge or Gelfoam is used.
- Moreover, intravenously administered applications like plasma expanders (e.g. Gelafundin™, Gelafusal™) consist of gelatin derivatives. Other uses of gelatin include sealants for vascular prostheses.
- It has been claimed that oral gelatin consumption has a beneficial therapeutic effect on hair loss in both men and women.

Gelatin in Nanopharmaceutics

- In terms of nanopharmaceutics, gelatin was considered as a interesting biodegradable base material in the early days of particle development. The gelatin nanoparticles are being explored for various therapeutic applications.
- Interest in use of gelatin as biodegradable materials are based on the facts that gelatin is FDA approved, biodegradable, non-toxic, easy to crosslink and to modify chemically and has therefore an immense potential to be used for the preparation of colloidal drug delivery systems such as nanoparticles.
- The gelatin nanoparticles are being used for variety of biomedical applications such as carriers for ophthalmic drugs, easy adherence to inflamed occular cells than normal cells.
- Gelatin nanoparticles have been used in therapeutic applications for diabetes, breast cancer, bladder cancer etc.
- Nanoparticulate carriers of gelatin have been used for efficient intracellular delivery of the encapsulated payload.
- Gelatin–DNA nanospheres have been described as a potent gene delivery vehicle.
- Nanoparticulate drug delivery system hold promising importance among the approaches used to deliver DNA due to their easy preparation, versatility.
- Gelatin hydrogels used as controlled release devices for a variety of growth factors known to enhance bone formation.
- Gelatin nanoparticles have been explored to encapsulate antitumor drugs, which resulted in increased efficiency, controlled release, and targeting of drugs to the affected area.
- Gelatin nanoparticles have been used as a carrier for gene delivery applications.
- Cationized gelatin nanoparticleshave shown the potential of being a new effective carrier for non-viral gene delivery.
- Nano-materials have been actively used in different applications like cancer therapy, drug delivery systems, tissue scaffolds, tissue engineering devices, diagnostics, and therapeutics in medicine.
- Gelatin-based nanoparticulate drug delivey systems have also used to deliver protein and peptide drugs.
- Moreover, gelatin nanoparticles have the ability to cross the blood-brain barrier, hence used as a promising tool to target brain disorders.
- Gelatin nanoparticles have been widely used as drug and gene carrier to targeted sick tissues including cancer, tuberculosis, due to its biocompatibility and biodegradability.
- Mannosylated gelatin nanoparticles could be useful as a carrier system in the treatment of macrophage-mediated intracellular infections.

Gelatin in photographic applications

- In the field of photography, gelatin was introduced in the late 1870s as a substitute for wet collodion. It was used to coat dry photographic plates, marking the beginning of modern photographic methods.
- Gelatin is the best medium known for making photographic emulsions.
- Gelatin is used as a component in a photographic developer during the processing of the exposed film material.
- Dichromated gelatin coatings are commonly used in production of high quality holographic images.
- Photographic technology offers a rapidly changing, highly sophisticated, very competitive market for photographic gelatin manufactures.

Gelatin in wound healing applications

- Gelatins A and B have been used as wound healing biomaterials in different forms.
- Gelatin can be used in various wound types that include partial and full-thickness wounds with exudate. There are several gelatin-containing wound dressings and haemostatic sponges on the market, such as DuoDerm®/Granuflex® (ConvaTec), which are hydrocolloid dressings that contain pectin and carboxymethyl cellulose in addition to gelatin; Gelfoam® (Pfizer), which is a sterile compressed sponge used as a hemostatic that is capable absorbing blood up to 45 times its weight.
- Although gelatin is an attractive wound healing biopolymer and is widely used in hydrocolloid dressings.

Gelatin micromolecules in therapeutic

- The novel applications of gelatin micro particles is in pulmonary diseases where it is used as aerosol.
- Negatively and positively charged gelatin microspheres were prepared using acidic gelatin and basic gelatin respectively.
- The average diameters of positively charged gelatin microspheres in their dried state 3.4, 11.2, 22.5 and 71.5 µm, while that of negatively charged gelatin microspheres was 10.9 µm.

Gelatin in tissue engineering [20, 21]

- Tissue engineering is one of the most interesting fields of nano-biotechnology.
- In tissue engineering gelatin is actively utilized for construction of biological and life-long 3D scaffolds for bio-artificial tissues and organ production.
- Presently various types of nanocomposites are tried in tissue engineering strategies, to make porous scaffolds.
- As gelatin is a denatured biopolymer, the selection of gelatin as a scaffolding material can circumvent the concerns of immunogenicity and pathogen transmission associated with collagen. Most of the work is based on the use of gelatin nano-composite focus in bone defects.

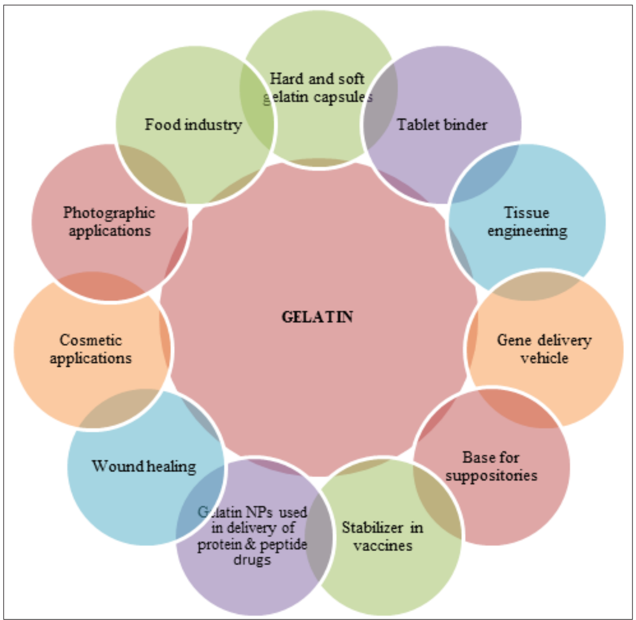

Figure 5: Applications of Gelatin

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