World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 7.409

MOLECULAR VERSATILITY AND BIOMEDICAL EXPLOITATION OF ALBUMIN: STRUCTURAL DYNAMICS, FUNCTIONAL ADAPTABILITY, AND TRANSLATIONAL APPLICATIONS

Mayuri Kalokhe*, Avadhut Khot, Aditya Jagtap, Vaishnavi Kolekar, Tejaswini Bhosale, Vedika Shinde

India.

***Corresponding Author: Mayuri Kalokhe**
India.

DOI: https://doi.org/ 10.5281/zenodo.17277362

Article Received on 21/08/2025 **Article Revised on 11/09/2025** **Article Accepted on 01/10/2025**

ABSTRACT
The most prevalent and adaptable plasma protein, albumin, is essential for preserving oncotic pressure, moving a variety of ligands, and preserving physiological homeostasis. An extensive review about albumin-related proteins, including their kinds, preparation techniques, and potential applications, is given in this article. Mobility, soluble status, and ligand-binding ability are important traits shared by all forms of albumin, even if manufactured albumin; this is bovine albumin, ovalbumin bovine plasma antibody (BSA), as well as human serum albumin (HSA) each have unique physicochemical properties. Ovalbumin is important within nutritional science and immunology, BSA is widely used in laboratory diagnostics, HSA is still essential in clinical applications, and recombinant albumin provides a scalable, pathogen-free option for therapeutic usage. Dissolving, emulsifying (evaporation and diffusion processes), thermal gelation, and enhanced nanoparticle creation are some of the technologies used to prepare albumin-based formulations. These techniques improve albumin's functional potential for application in therapeutic platforms, drug delivery systems, and diagnostics. Albumins are excellent prospects for cutting-edge biomedical applications because of their inherent stability, biocompatibility, and modifiability. The latest advances in genetic modification, protein editing, and nanotechnology should open up new uses for albumin in medicine and industry. These developments will make it possible to create new therapeutic agents, targeted delivery methods, and more effective drug carriers. All things considered, albumins are an essential section of multimodal proteins whose versatility guarantees their ongoing significance in biotechnology, medicine, and scientific study.

KEY WORDS: Albumin, HSA, or human serum albumin, Nanoparticles of albumin, Delivery of Drugs, Method of Desolvation, Methods of Emulsion, Engineering Proteins, Nanomedicine.

1. INTRODUCTION

In pharmaceutical applications, nanotechnology has great promise, especially for the delivery of medications. One Effective treatment, protection, delivery, and transportation of difficult therapeutic or diagnostic cargos—such as poorly soluble medications, proteins, and gene therapies—to subcellular along with intracellular regions in biological fluids are made possible by nanomaterials.[1] Smart nanostructured materials can transport medications to target locations in a regulated manner, reducing adverse effects compared to traditional therapies.[2] Because of its exceptional binding ability between hydrophobic and hydrophilic medicines, long half-life, precise targeting of inflammatory areas, low toxicity, and little immunogenicity, albumin, which is a plasma protein, has been recognized as a natural and adaptable nanodelivery system.[3] The science of manipulating matter that is one nm or smaller is known as nanotechnology (1). A lysosome can be 200–500 nm and width, a strain of E. Coli bacteria measures roughly 2 µm long, a H atom is 0.1 nm in diameter, and the majority of eukaryotic cells are 8–30 µm in diameter or more.[4] Researchers have identified albumin, a naturally occurring protein in blood plasma, as a flexible nano delivery method. This method is appealing due to its ability to attach either hydrophilic or hydrophobic medicines, increase its longevity in the body, target inflammation locations precisely, and have minimal toxicity or immune response potential.[5] The following features of an effective drug delivery nanodevice should be met: targeted distribution to disease locations, prolonged circulation time, immune system evasion, and drug retention. Releasing the drug and preventing the most important organs. Targeted ligand-enriched nanodevices are employed in nanomedicine to reduce side effects at low therapeutic

levels.[6] Designing, developing, evaluating, and utilising devices and materials having operational structure at the nanoscale (one thousandth of a meter) is the focus of nanotechnology. In recent years, the multidisciplinary field of nanotechnology has grown rapidly.[7] Research can yield significant health advantages. Nanotechnology began with the potential of revolutionary advancements in medicine, communications, genetics, and robotics.[8] Nanotechnology platforms are being studied in both development and clinical stages to improve therapeutic efficacy and safety for many purposes. New cancer treatment solutions have been launched, addressing a critical need. Nanoparticle medicines have the potential to significantly improve oncology treatment.[9]

The system of reticuloendothelial cells (RES) plays a significant role in nanoparticle survival in circulation. Recognizing a foreign antigen can trigger phagocytosis and activation of immune systems, including the generation of high-affinity antibodies by B-2 cells.6 Acquiring antibodies improves particle clearance by opsonizing, activating the system of complements, and inducing an inflammatory response, which may lead to hypersensitive reactions.[10]

2. TYPES OF ALBUMIN

Ovalbumin

Ovalbumin (OVA), the main protein fraction of poultry eggs, is the first protein separated into monomers in egg white (Zhu et al. 2018). OVA has attracted increasing interest for its good functions, including gelling, foaming and emulsifying properties.[11] With 385 amino acids, more than half of which are hydrophobic, ovaalbumin is a single peptide chain with a relative molecular mass of 45 kDa.

[12]Providing a range of modular systems for assessing the pharmacokinetic behavior, adjuvant function, encapsulation efficiency, and other preferred biological reactions of nanocarriers.[13] Additionally, during storage, it changes into the heat-stable form S-ovalbumin. Temperature and pH are both factors that alter during storage and have an impact on the production of S-ovalbumin. As a result, S-ovalbumin is acknowledged for having the ability use as a reference measurement for indicating the state of freshness of commercial eggs.[14] Initially, saturated monium sulfide as well as acetic acid were used to isolate albumin; however, there is no precise record of its production or purity. Ovalbumin was recently isolated using liquid chromatography, foam fractionation, or a dual-stage polyurethane thin disk membrane electrophoretic approach. However, because of their intricate processes, high material costs, and sample handling requirements, all of these methods are challenging to scale up for industrial applications.[15]

Human Serum Albumin

With all endogenous and exogenous substances, HSA acts as a store and transporter due to its exceptional ligand-binding ability. In fact, HSA is the primary transporter of fatty acids (FA), influences the pharmacokinetics of numerous medications, offers the metabolic modulation of some ligands, neutralizes possible poisons, makes up the majority of human plasma's antioxidant capacity, and exhibits (pseudo-) enzymatic qualities.[16] Serum albumin from humans (HSA), or simply albumin, is one of the readily purifiable biological compounds that may be created at the nanoscale. It is widely distributed and found in both liquid and solid tissues. Throughout World War II, albumin was initially used in medicine as a blood substitute and later as a cirrhosis cure.[17] One of the easily purifiable biological materials that can be produced at the nanoscale is human serum albumin (HSA), or simply albumin. It is present in both solid and liquid tissues and is ubiquitous. Albumin's clinical application began during World War II, first as a plasma substitute and then as a treatment for cirrhosis.

Although it has a large negative charge, albumin binds a variety of both negatively and positively charged molecules. Water-resistant organic compounds such hemoglobin as well as long-chain fatty acids are among them, as are bivalent (as well as monovalent), charges like calcium and magnesium. Acids from bile, copper, zinc, many medicines, and even chemicals with specific serum binders, such as vitamin D and thyroxin, are among the other physiologically important substances bound by albumin.[18]

Bovine Serum Albumin

Currently, BSA and HSA share 76% of their similarities, making them the most commonly utilized polypeptide templates for biophysical and biochemical research. BSA has 582 amino acid residues, Twenty tyrosyl chain molecules (Tyr), as well as 2 trypsin complexes (Try), which are found at places 135 (subdomain IA) and 212, respectively (subdomain IIA), according to the crystal structure analysis.[19] Because of its well-known fundamental structure and capacity to bind a wide range of tiny molecules, such as dyes, drugs, and dangerous compounds, protein from bovines (BSA), one of the main parts of plasma protein, is frequently utilized for biophysical and biochemical investigations.[20] When two or more water-soluble solutes dissolve in aqueous solution, ABS is produced. Typically, this involves two polymers substances, a polymer plus salt, or two salts. At larger concentrations, phase separation happens. DNA, RNA, protein amino acids, antibodies, enzymes, and other living materials and chemicals have been all extracted and purified utilizing traditional polymer-based ABS.

In typical polymer-based ABS, the existing phases have minimal polarity differences, making it unable to achieve significant extraction efficiencies and selectivities in a single step. Later, it was proposed to replace polymer-based ABS with ionic-liquid-based (IL-based) ABS, which has numerous advantages. Usually, these ABS's lower viscosity and faster phase separation rates lead to

higher extraction efficiencies. As well as generally lead to higher extraction efficiency. Regular salts have higher melting temperatures than ILs, which are made up of a specific inorganic or organic, anion and a certain organically cationic anion.Often called "designer solvents," most ILs have strong solvation capabilities for a variety of molecules, good thermal and chemical stabilities, minimal volatility at atmospheric conditions, and the ability to conjugate ions according to the intended use.[21]

3. STRUCTURE AND PROPERTIES OF ALBUMIN

With concentrations of about 0.6 mmol/L, albumin normally accounts for about 50% of plasma's total protein content. HSA is a small, globular protein of 584 amino acids that weighs only 66 KD. Instead of carbohydrate or elastomeric groups, there are a number of charged residues, such as lysine and aspartic acids, together with tryptophan or methionine residues. Because HSA is ellipsoid in solution, X-ray crystallography shows that protein displays a heart-shaped tertiary structure. Around sixty-seven percent of the human serum albumin tertiary structure is composed of helices.The protein is really composed of 3 homology domain (I to III), each of which contains a pair of subdomains (A as well as B), every of which has 4 and 6 helices, respectively.[22] Malnutrition and heart failure can occasionally cause low albumin (hypoalbuminemia), while heart failure and other factors can cause high albumin (hyperalbuminemia).

Burn, vitamin insufficiency, etc. Albumin has a variety of energy functions. The distribution of lipids and bilirubin depends critically on the mechanical capacity of the blood, which is caused by the amount of albumins in blood vessels. It is composed of a single chain of about 580 residues connected by peptide links.[23]

It is made up of a single 585 amino acid polypeptide chai n having a molecular mass of 66 500 Da

Its mature and circulating molecule is kept together by 1 7 disulphide bridges and is organized in a sequence of α-helices.

Three parallel contiguous α-helices are formed as subdomains by the folding (Fig. 1).

Domains are made up of two subdomains facing one anot her.

These resemble cylindrical formations with a hydrophobi c core and polar exterior walls.[24] Because of these pockets, albumin may attach to a wide range of compounds, such as fatty acids:
Bile acids
Drugs, Metals, Hormones, and Toxins
Because of its unique structure and functional groups on its surface, albumin can bind to a variety of substances. These functional groups have the ability to form ionic and hydrogen connections and have hydrophobic interactions with surrounding molecule.[25]

4. FUNCTION OF ALBUMIN

HSA has a wide range of functions, including stabilizing endothelium, modifying capillary permeability, preserving plasma oncotic pressure, solubilizing, legally binding, and carrying naturally occurring and exogenous molecules, and having hemostatic, anti-oxidative, and anti-inflammatory effects. The distribution and structure of dynamic functions HSA are impacted by the concentration.[26]

Preserving Fluid Balance

Think of albumin as your blood's microscopic sponge. The size as well as negative charge make it appealing. Water molecules, generating strong **colloid osmotic pressure** that pulls fluid into the blood vessels through the interstitial cavity (between cells). This keeps fluid from building up in tissues, or edema, and helps maintain blood volume. Imagine it as a dam that keeps water from leaking out, making sure the proper volume of fluid remains inside the blood arteries.[27]

Solublization, binding, and transport of molecules

Fatty acids are essential to the mammalian body because they are the building blocks of cellular membranes, signal transducers, and sources of chemically stored energy.[28] Many physiological functions depend on HSA's ability to bind molecules, which can increase the solubility of a variety for endogenous and exogenous substances in plasma and facilitate their movement or detoxification. The three-dimensional structure of HSA dictates how well it binds other substances. With an overall molecular weight of of 66,438 and 585 amino acid residues, it is a macromolecule. His tertiary structure is heart-shaped, with several a-helices, each with two homologous domains (I–III).

A and B are subdomains. This specific structure is stable and flexible, and it may be easily changed, enabling the molecule to incorporate a variety of compounds with strong protein-binding capabilities. Furthermore, certain substances alter the three-dimensional structure of the macromolecule and vie on HSA binding sites, which affects the functionality of the macromolecule.[29] Following passage through the intestinal epithelial cells' luminal membrane, the breakdown products undergo resynthesis to triacylglycerols, are then combined to form chylomicrons, and are then sent to the lymphatic system via the epithelium's basal membrane.[30]

Antioxidant function

Up to 60% of all blood proteins are Albumin is a 66 kDa non- glycosylated protein with a normal plasma concentration of 35–50 g/l. In normal situations, its half-life is about 20 days. The main ligands of HSA involved in the either the indirect or direct antioxidant actions of the protein are transition metal ions, primarily copper

and iron. The high affinity area for Cu (II) ions is composed of the first four amino acids in the Asp-Ala-His-Lys (DAHK) region of the N-terminus of HSA. Free redox-active transition metal ions Cu (II) and Fe (II) have the potential to be very pro-oxidant.[31]

Anti-inflammatory properties

To determine whether 25 percent human being albumin is an effective rescue liquid and an immune-modulating agent that protects toward injury to the lung in our model, and to evaluate potential new uses of human albumin in solution solutions in the management and prevention of acute lung damage after shock or resuscitation.[32] Research suggests that, depending on their redox state, accessible groups of thiol can signal regulatory changes in inflammatory cells. HSA influences the activation of the global gene transcription nuclear factor-kappa B and raises intracellular glutathione levels using both in vitro and in vivo methods. Additionally, several recent studies using an animal model of hemorrhaging shock have shown that proinflammatory responses, including neutrophil activation rates and lung apoptosis, are significantly influenced by the kind of restorative fluid employed. Plasma albumin was shown to be the least pathogenic of the fluids used. The formation of sulfuric acid residue through cys-34 oxidation15 might be an essential element regulating signaling responses, according to recent studies that indicates these groups have an effect on cellular signaling activities.[33]

5. CHARCTERISTICS OF ALBUMIN FROM DIFFERENT SPECIES

Serum albumin (SA) is one of the most common molecules in the blood plasma which is easily found in the body of a living organism.

They move proteins, scavenge free radicals, and regulate osmotic pressure.[34] Human serum albumin (HSA), which has a theoretically pI of 5.12, is made up of 83 positively charged residues (Arg + Lys) and 98 negatively charged ones (Asp + Glu). Albumins are commonly seen in blood plasma and are not glycosylated like other blood proteins. Several additional plasma transport proteins, including alpha-fetoprotein, a vitamin D-binding protein, as well as afamin, have evolutionary ties with serum albumin.[35] The most common plasma protein, albumin (35–50 g/L human blood), is produced by the liver at a rate of roughly 0.7 mg/h per gram the liver, or 10–15 g daily. An acidic protein, albumin is soluble in 40% ethanol, constant between pH 4 and pH 9, and is resistant during heating to feed up to 10 hours at 60°C. It is also very soluble (up to 40% w/v) on pH 7.4. These qualities, along with its availability, immunogenicity, biocompatibility, biodegradability, and lack of toxicity, make it the ideal choice for drug delivery.[36] Although it can be obtained from a number of sources, including human albumin (human serum albumin, HSA) (Figure 1), bovine albumin (bovine serum albumin, BSA), rat serum albumin (rat serum albumin, RSA), & egg white (ovalbumin, OVA), the two most popular types for drug administration are HSA10 and BSA.

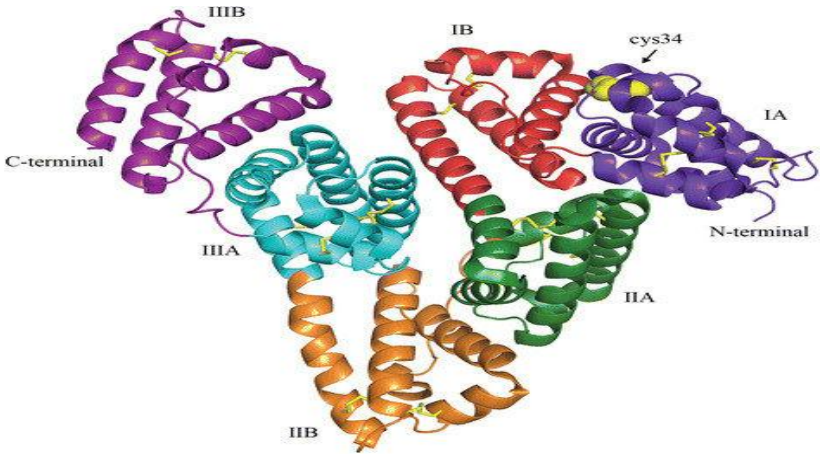

Figure 1: The domain organization and structural properties of human serum albumin (HSA).

Albumin is defined by three categories (I, II, and III), as seen in Figure 1. Each domain is composed of 2 subdomains (A and B), each of which has four α helices. Located in categories IIA and IIIA, respectively, Sudlow sites I and II, 12 are the most important human serum albumin binding sites on hydrophobic compounds, especially those with charges that are neutrally as well as negatively charged. These domains are incredibly lengthy hydrophobic pockets that have lysine and arginine residues that are positively charged. 13. Site I is notably known as the warfarin site because drugs such as phenylbutazone, azapropazone, & warfarin bind to it. Site II is also sometimes referred to being a benzodiazepine site since it is where drugs like diazepam, ibuprofen, as well as tryptophan bind. Because substances like diazepam, ibuprofen, along with tryptophan bind to Site II, it is often referred to as a benzodiazepine site. This allows for the successful binding and subsequent delivery of several medicines, including docetaxel and paclitaxel, to the malignancy site.[37]

6. SERUM ALBUMIN FROM OTHER SPECIES

Serum albumin has been the subject of the greatest research of any protein. According to the species, it is a single protein having 580–585 amino acid repeats in a single peptide chain. Due to the absence of a carbohydrate component, the polypeptide chain has low levels of tryptophan (1–2 residues) & methionine (4–6 residues).

On the other hand, lysine, arginine, glutamate and aspartic acids, and many other charge amino acid residues are found in albumin. A distinctive arrangement of double loops joined by disulfide bridges makes up the secondary structure.

These nine loops consist of the amino acid sequences 1-190, 191-382, and 383-585 and repeat of a triplet pattern on human albumin.[38] Numerous vaccinations, including MMR, MMRV, Varicella, and Zoster, contain BSA[16, 17], and it is a crucial component of the cell culture medium used for artificial insemination. Because of its allergenicity, BSA is also being researched; it has been found to be a mild allergen in bovine serum and dander.[39] The significant differences among HSA and BSA are illustrated in two places within the subdomain IB. Most of the different residue remain visible near the protein's outermost layer in the first region, which is made out of residue 114 to 135 (numbered in respect to mature BSA) and is situated around the first two α-helices on the IB subdomain.[40] HSA, which is commonly known as "chronosteric effects," demonstrates heme-based catalytic properties that are time-dependent. The significance of HSA for the movement of iron macrocycles from low-density lipoproteins and high-density lipoproteins to hemopexin, with confers globin-like reactivity, is demonstrated by this. Through CD91 receptor-mediated endocytosis, the hemopexin: heme complexes enters the hepatic parenchyma and releases the recycled or degraded heme. Normally, HSA-hemeFe (III) plasmatic amounts are around $1.0 \times 10{-}6$ M; however, in those with serious hematologic diseases, these levels can reach a maximum of about$4.0 \times 10{-}5$ M.[41]

7. PREPARATION METHODS OF ALBUMIN NANOPARTICLES

The internal circulatory of nanoparticle drug carrier systems is influenced by two main physicochemical factors: particle size and surface characteristics. A capillary network's particles should be small enough to avoid being removed by simple filtration techniques. Intravenous delivery the process of amino acid adsorption upon particle surfaces paired with monocyte & macrophage identification of these coated particles is known as optonization. This opsonization process seems to be influenced by the surface curvature on the carrier system; smaller carriers lead to reduced adsorption of proteins and opsonins, which in turn decreases the absorption of these systems the phagocytic cells.[42] The amino moieties in the albumin's residues of lysine as well as the guanidino reactions within its arginine residues are solidified by a condensation reaction involving the glutaraldehyde aldehyde group. The nanoparticles are purified by centrifugation, which gets rid of extra cross-linking agent, ethanol, including unreacted albumins. By freeze-drying the resultant nanosuspension containing 5% mannitol added as a cryoprotectant, the nanoparticles are reduced to a finely ground powder. Glutaraldehyde remains in the form of nanoparticles and has a number of negative impacts. On the other hand, EDC is a zero-space cross-linker.[43] The pharmaceuticals can be encapsulated in the NPs using a variety of techniques, such as desolvation, thermal gelation, self-assemble emulsification, and nanospray-drying.[44]

I. Desolvation (Coacervation)

The Dissolution the first step in the manufacture of albumin nanoparticles is the desolvation process.41 this technique involves gradually adding organic solvents that dissolve in water, like ethanol, to a diluted albumin solution while stirring continuously. Phase-based separation results from albumin being less soluble. Since albumin particles continue to be entirely stable at this point and could return to the aqueous phase, a substance called crosslinker needs to be added to increase the flexibility of the generated nanoparticles. Cross linking of desolvated particles is an important step in the synthesis of albumin nanoparticles, and it affects the durability, biodegradability, and drug release through the carrier system. This procedure involved combining the solution of albumin with the dissolving agent (drug solution) to create NPs. When the medicine solution was added, albumin's solubility in the medium decreased. In addition to NP synthesis and albumin molecule polymerization, drug molecules was trapped. The NPs were made stable after 15 hours via the addition of 8% (v/v) water glutaraldehyde into the solution. To analyze the process and characterize the most fruitful components, the tests were designed using CCD-RSM. The mean particle size.[45]

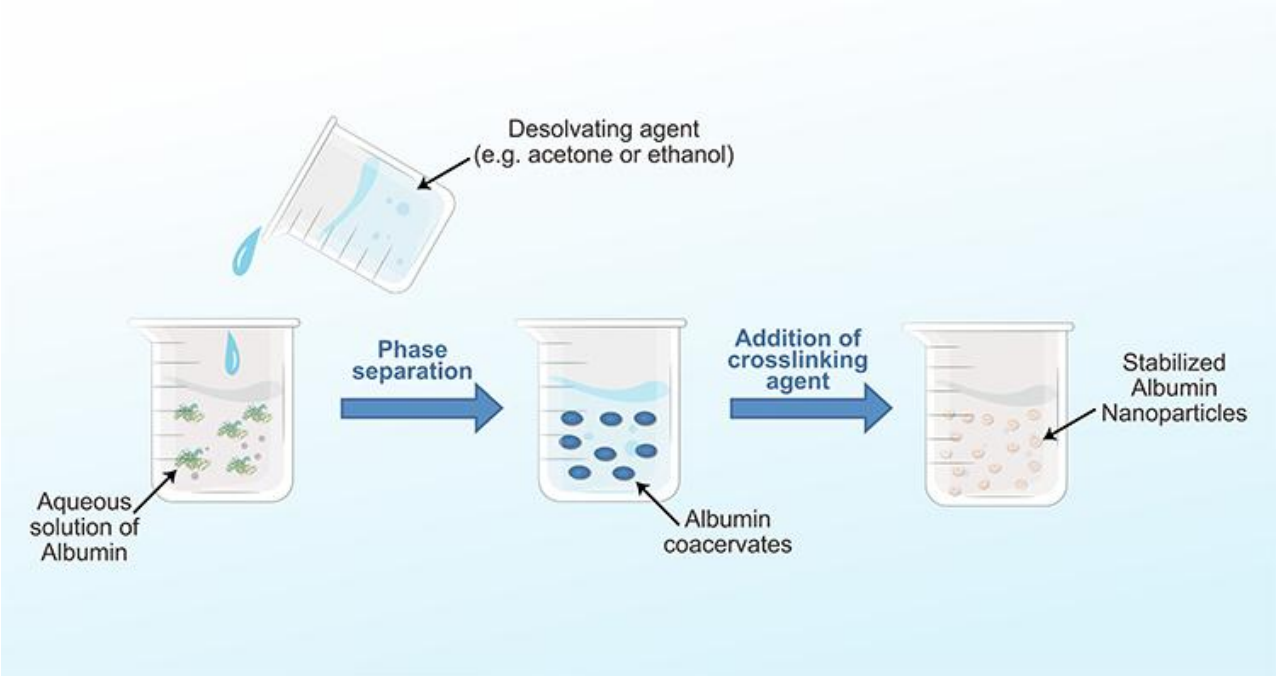

Figure 2: "Desolvation Method for Albumin Nanoparticle Preparation".

II. Emulsification

Emulsification is another widely used technique that uses nano- and predominantly microemulsions have surfactant-stabilized droplets to create NPs of median diameters of 100–1000 nm. Emulsification requires organic solvents, and removing the surfactants and oily residues may be difficult. However, the procedure can encapsulate hydrophilic and hydrophobic medications, based on whether the one or dual-emulsion technique was employed. Drug delivery has been tried with a variety of drugs. Protein nanoparticles are created into nanospheres by alternatively suspending them inside of oil using an ultrasound shear or by forming the particles at the water-oil interface of the solution using a high-speed homogenizer. Surfactants such as phosphatidylcholine, sodium dodecyl sulfate, or Span 80 are utilized to stabilize the particles. Protein nanoparticles created using an emulsion process are joined by thermal cross-linking for 20 minutes at 60°C or by adding glutaraldehyde (chemical crosslinking). For certain proteins, such albumin or whey proteins, the pellets are then washed with ethanol after the fluid has been centrifuged. The emulsion process is composed of two steps: emulsion diffusion, which starts when the polymer (protein) entirely dissolves in the solvent (oil) under extreme shear stress. The stabilizer solvent (sodium dodecyl sulphate) is then added, and everything is well mixed with a magnetic stirrer. The particles are taken out of the aqueous phase by nanoprecipitation. The steps in the emulsified diffusion technique are shown in Figure 3. The second process, called emulsion solvent evaporation, involves dissolving proteins (casein and albumin) in appropriate solvents (such methanol or chloroform). To produce stable emulsified droplets, the protein solution and surfactant are subsequently mixed together using a magnetic stirrer as well as a powerful shear force. The organic solvent present in the droplets is removed under vacuum. The nanoparticles are then produced by nanoprecipitation. The scheme for the evaporation process is shown in Figure 4.[47]

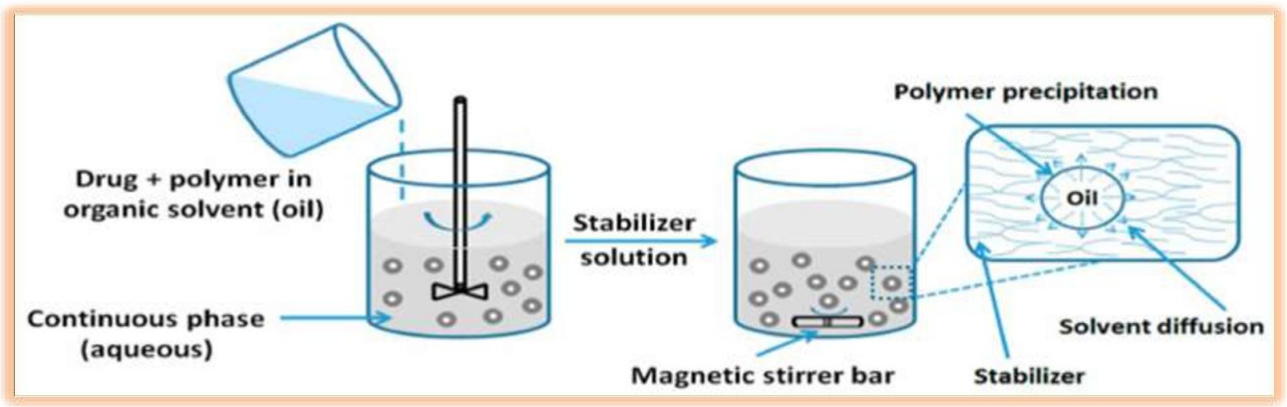

Figure 3: Formation of Protein Nanoparticles via Emulsion-Based Solvent Diffusion.

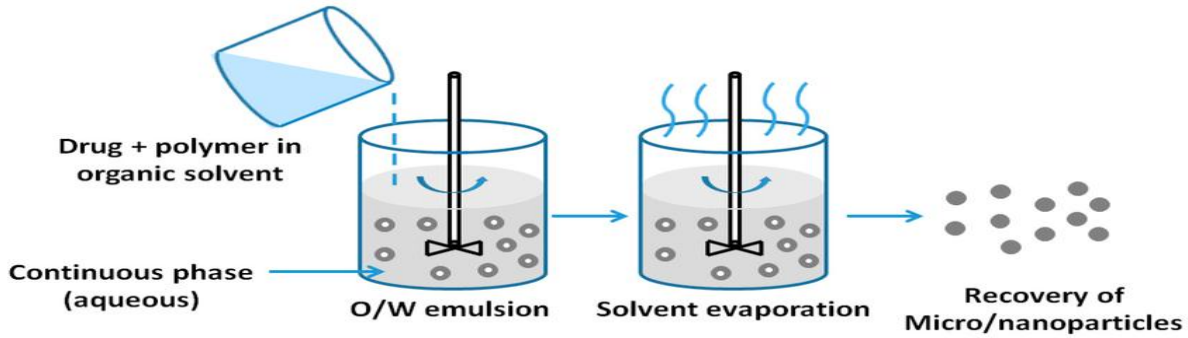

Figure 4: Formation of Polymeric Nanoparticles via Emulsion Solvent Evaporation.

III. Nanospray drying

There are three primary ways to create nanoparticles: (i) Physicochemical techniques, which include emulsifying premade polymers to cause them to precipitate; (ii) mechanical techniques, including spray-drying; and (iii) in situ chemical synthesis techniques for macromolecules, like polymerization or interfacial polycondensation reactions Spray-drying is the process of turning a liquid into a dry powder by disintegrating a solution, emulsion, and suspensions onto a hot dried gas medium, often air. Depicts the four fundamental processes of the spray-drying process: (i) atomizing the liquid feed to create a spray; (ii) mixing hot gas stream with spray droplets; (iii) evaporating liquid to create dry particles; and (iv) gathering dry particles.[48] In particular, pure, poorly water-soluble drugs, such as dexamethasone, anti-inflammatory, and others, can be directly transformed into submicron powders by nano spray drying. 33. Anti-inflammatory drug/indomethacin, 85. Mecigestone, steroidal hormone, 153 or Nimes Lide, analgesi, 154 or nicergoline, vasodilator, 58. Diuretic or furosemide.[48] Spray-drying is the process of converting a liquid into a powder. The four processes of a typical spray drying process are material atomization, gas drying, particle creation, and particle collection. Some benefits of spray-drying include a straight forward production method, quick drying times, and good product dispersion.

As a result, it is extensively utilized in dairy products, de tergents, medicine, and other industrie However, The traditional spray-drying equipment struggles to capture particles less than 2 μm, whereas the hot air drying process is easy to denature.and deactivate albumin, making it unsuitable for albumin nanoparticle production. The albumin nanoparticles made using the spray-drying approach frequently exhibit substantial drug loading, and the steps involved are rather straightforward. Chow et al. developed high siRNA loading powders based on HSA using the spray-drying process[49] it involves atomizing the feed into a spray, combining it with air, drying the spray, and then separating the dried product from the drying air, among other process processes. When the liquid feedstock comes into contact with a drying gas that is hot enough to promote moisture evaporation, a spray of droplets is created. An aqueous albumin solution in a drying chamber is where this interaction takes place.[50]

IV. Self Assembly method

Another popular technique for producing albumin NPs is self-assembly. The HSA self-assembles and forms micelles when a lipophilic drug is given and the protein's surface amine group count is decreased, making albumin more hydrophobic.[33] In this case, a study exposed BSA to argon and mixed it with succinylated cholesterol. The cholesterol (Chol)–BSA was dissolved, then paclitaxel was added gradually while stirring to generate the albumin–drug composite (paclitaxel–Chol–BSA). The NPs displayed an excellent drug-loading capacity and a hydrodynamic diameter of 147.6 ± 1.6 nm. Paclitaxel-Chol-BSA NPs demonstrated prolonged drug release and were an effective agent.[51]

V. Thermal Gelation

Protein interactions, including hydrophobic, electrostatic, and hydrogen bonding interactions, as well as thermally induced unfolding, are all part of the ongoing process of thermal gelation. This method's benefits include its ease of use and the absence of the necessity for crosslinking chemicals, as well as the good stability of the albumin nanoparticles it produces. The drawback is that they are incompatible with medications that are heat-sensitive. Because they are relatively stable, albumin nanoparticles made by thermal gelation frequently exhibit good mechanical qualities. Hughes et al. used thermal gelation to create albumin-based nanoscale hydrogels, which had good mechanical qualities.[52]

8. FUTURE PRESPECTIVE

Its advantages—long lifespan, non-toxicity, non-immunogenicity, and good biocompatibility—have attracted a lot of attention to research on drug delivery systems. Thanks to the important developments in nanomaterials for HSA nanocrystallization and the naturally occurring binding sites of HSA, therapeutic drugs can be effectively coupled via HSA or encapsulated inside HSA nanoparticles. Small-molecule drugs, inorganic materials, and bioactive ingredients (peptides, enzymes, cytokines, antibodies, & nucleic acids) make up these drugs. They help to improve therapeutic efficacy, systemic stability, and pharmacokinetics while lowering systemic side

effects.[53] Our knowledge of albumin biology as well as the biology of cirrhosis and its complications has drastically changed over the last 20 years. The main aspect of cirrhosis that has not yet been acknowledged is that it is a condition of systemic inflammation that is exacerbated in patients who have problems, especially those with ACLF. The significance of albumin therapy, which corrects circulatory malfunction and regulates inflammation, in patients with liver disease is amply demonstrated in the sections above. Along with the use from albumin to manage SBP66, HRS68, and prevent post-paracentesis circulatory dysfunction, the recent notion that prolonged outpatient albumin therapy may increase their longevity is prompting a tailored strategy to albumin substitution and optimization.[54]

CONCLUSION

The most prevalent and adaptable plasma protein, albumin, is essential for preserving oncotic pressure, moving a variety of ligands, and preserving physiological equilibrium. Although each of the various types of globulin—human serum albumin, which is animal serum albumin, synthetic albumin, as well as ovalbumin—has distinct biochemical qualities, they all have solubility, stability, and the ability to bind ligands. Bovine serum albumin is widely used in medical research and diagnostics; human albumin from the blood is still necessary in clinical settings; ovaalbumin is crucial in protein science, the immune system, and food science; and recombinant albumin provides a scalable and pathogen-free alternative. Together, these albumins demonstrate the wide range of uses for this protein family in business, biotechnology, and medicine.

Albumins are perfect macromolecules for enhanced biotechnological advancements, delivery methods for drugs, and therapeutic interventions because of inherent physical balance, antioxidant potential, and structural modification ability. New clinical and industrial uses are made possible by the ongoing advancements in gene editing, protein engineering, and nanomedicine, which expand their reach and get past long-standing constraints. All things considered, albumins are an essential class of proteins whose versatility and multifunctionality guarantee their ongoing importance in applied medicinal research as well as scholarly studies.

REFERANCE

1. Spada A, Emami J, Tuszynski JA, Lavasanifar A. The uniqueness of albumin as a carrier in nanodrug delivery.
2. Lombardo D, Kiselev MA, Caccamo MT. Smart nanoparticles for drug delivery application: Development of versatile nanocarrier platforms in biotechnology and nanomedicine. Biotechnol Nanomedicine. [Journal name placeholder] [Year]; [Volume(Issue)]:[Page numbers]
3. Spada A, Emami J, Tuszynski JA, Lavasanifar A. The uniqueness of albumin as a carrier in nanodrug delivery. Molecular Pharmaceutics, 2021 May 3; 18(5): 1862–1894.
4. Wang S, Su R, Nie S, Sun M, Zhang J, Wu D, Moustaid-Moussa N. Application of nanotechnology in improving bioavailability and bioactivity of diet-derived phytochemicals. J Nutr Biochem., 2014 Apr; 25(4): 363–376. AGRISPubMed
5. Nandale DD, Pathan MA, Pansare JJ, Patil CG, Gavhane AA, Jadhav SP. Albumin as a carrier in nanodrug delivery system: a review. Human Journals, 2024 March; 30(3). Research Gate
6. Loureiro A, Azoia NG, Gomes AC, Cavaco-Paulo A. Albumin-based nanodevices as drug carriers. Curr Pharm Des., 2016; 22(10): 1371–1390. doi:10.2174/1381612822666151211115643
7. Sahoo SK, Parveen S, Panda JJ. The present and future of nanotechnology in human health care. Nanomedicine, 2007; 3(1): 20–31. doi:10.1016/j.nano.2006.11.008
8. Sahoo SK, Parveen S, Panda JJ. The present and future of nanotechnology in human health care. Nanomedicine: Nanotechnology, Biology and Medicine, 2007 Mar; 3(1): 20–31. doi:10.1016/j.nano.2006.11.008 ResearchGateUW-Madison Librariesscilit.net
9. Lohcharoenkal W, Wang L, Chen YC, Rojanasakul Y. Protein nanoparticles as drug delivery carriers for cancer therapy. Biomed Res Int., 2014; 2014: 180549. doi:10.1155/2014/180549
10. Ziv O, Avtalion RR, Margel S. Immunogenicity of bioactive magnetic nanoparticles: natural and acquired antibodies. Acta Biomater, 2008; 4(1): 66–79. doi:10.1016/j.actbio.2007.06.008
11. Ma B, Fu X, Zhu P, Lu Z, Niu J, Lu F. Allergenicity, assembly and applications of ovalbumin in egg white: a review. Crit Rev Food Sci Nutr., 2024; 64(24): 8672–8688. Published online 25 April 2023. Taylor & Francis Online
12. Zhao Y, Chen Z, Li J, Xu M, Shao Y, Tu Y. Formation mechanism of ovalbumin gel induced by alkali. Food Hydrocolloids, 2016; 61: 390–398.
13. Pang G, Liu Y, Wang Y. Endotoxin contamination in ovalbumin as viewed from a nano-immunotherapy perspective. WIREs Nanomed Nano bio technol, 2022; 14(1): e1747. First published 10 August 2021. Wiley Online LibraryPubMed
14. Maggonage HU, Manjula P, Ahn DU, Abeyrathne EDNS. Ovalbumin: A potential functional protein. Food Sci Preserv., 2024; 31(3): 346–359. American Chemical Society Publicationsekosfop.or.kr
15. Abeyrathne EDNS, Lee HY, Ahn DU. Sequential separation of lysozyme, ovomucin, ovotransferrin, and ovalbumin from egg white. Poult Sci., 2014 Apr; 93(4): 1001–1009. doi:10.3382/ps.2013-03403. PubMedOUCI
16. Fanali G, di Masi A, Trezza V, Marino M, Fasano M, Ascenzi P. Human serum albumin: from bench to bedside. Mol Asp Med., 2012; 33(3): 209–290. doi:10.1016/j.mam.2011.12.002 PMCEurope PMCOUCI

17. Zeeshan F, Madheswaran T, Panneerselvam J, Taliyan R, Kesharwani P. Human serum albumin as multifunctional nanocarrier for cancer therapy. J Pharm Sci., 2021; 110(9): 3111–3117. doi:10.1016/j.xphs.2021.05.001 ouci.dntb.gov.ua
18. Levitt DG, Levitt MD. Human serum albumin homeostasis: a new look at the roles of synthesis, catabolism, renal and gastrointestinal excretion, and the clinical value of serum albumin measurements. Int J Gen Med., 2016; 9: 229–255. doi:10.2147/IJGM.S102819 Taylor & Francis Onlinedovepress.compmc.ncbi.nlm.nih.gov
19. Behera S, Mohanty P, Dash PP, Mohapatra P, Shubhadarshinee L, Behura R, Barick AK, Mohapatra P, Jali BR. Selective binding of bovine serum albumin (BSA): a comprehensive review. Biointerface Res Appl Chem., 2023; 13: 555. doi:10.33263/BRIAC136.555 SpringerLinkOUCI
20. Zhang G, Zhao N, Hu X, and Tian J. Interaction of alpinetin with bovine serum albumin: probing of the mechanism and binding site by spectroscopic methods. Spectrochim Acta A Mol Biomol Spectrosc., 2010 Aug; 76(3-4): 410–417. doi:10.1016/j.saa.2010.04.009. Europe PMCui.adsabs.harvard.edu
21. Rufino AFCS, Almeida MR, Sharma M, Coutinho JAP, Freire MG. Separation of albumin from bovine serum applying ionic-liquid-based aqueous biphasic systems. Department of Chemistry, CICECO-Aveiro Institute of Materials, University of Aveiro, 3810-193 Aveiro, Portugal; Indian Center for Climate & Societal Impacts Research (ICCSIR), VRTI-Campus, Nagalpur Road, Mandvi, Kachchh, Gujarat 370 465, India.
22. Quinlan GJ, Martin GS, Evans TW. Albumin: biochemical properties and therapeutic potential. Hepatology. [Year]; Volume
23. Kajal, Pathania AR. Chemistry behind Serum Albumin: A Review. E3S Web of Conferences. 2021; 309: 01086. DOI: 10.1051/e3sconf/202130901086 E3S Conferences
24. Nicholson JP, Wolmarans MR, Park GR. The role of albumin in critical illness. Br J Anaesth., 2000; 85(4): 599–610. doi:10.1093/bja/85.4.599
25. Gupta Y, Rai V, Singh A, Khan S, Bano N, Yadav R. The uniqueness of albumin as a carrier in nano drug delivery. Int J Pharm Sci Drug Res. [Year]; [Volume(Issue)]
26. Sun L, Yin H, Liu M, Xu G, Zhou X, Ge P, Yang H, Mao Y. Impaired albumin function: a novel potential indicator for liver function damage? Ann Med., 2019; 51(7-8): 333–344. Available from: https://www.tandfonline.com/doi/pdf/10.1080/07853890.2019.1693056
27. Gupta Y, Rai V, Singh A, Khan S, Bano N, Yadav R. The Uniqueness of Albumin as a Carrier in Nano Drug Delivery. J Pharm Pharmacol., 2025; 15(4): 123–130.
28. VanderVusse GJ. Albumin as fatty acid transporter. Dept of Physiology, Cardiovascular Research Institute Maastricht, Maastricht University, Maastricht, the Netherlands.
29. Sun L, Yin H, Liu M, Xu G, Zhou X, Ge P, Yang H, Mao Y. Impaired albumin function: a novel potential indicator for liver function damage? J Hepatol Res., 2023; 45(3): 215–22.
30. Van der Vusse GJ. Albumin as fatty acid transporter. Dept of Physiology, Cardiovascular Research Institute Maastricht, Maastricht University, Maastricht, the Netherlands.
31. Taverna M, Marie AL, Mira JP, Guidet B. Specific antioxidant properties of human serum albumin. Biochim Biophys Acta., 2013; 1830(12): 5465–72.
32. Powers KA, Kapus A, Khadaroo RG, He R, Marshall JC, Lindsay TF, Rotstein OD. Twenty-five percent albumin prevents lung injury following shock/resuscitation. Crit Care Med., 2003 Sep; 31(9): 2355–63.
33. Quinlan GJ, Martin GS, Evans TW. Albumin: biochemical properties and therapeutic potential. Hepatology, 2005 Jun; 41(6): 1211–9. doi:10.1002/hep.20720.
34. Nurdiansyah R, Rifa'i M, Widodo. A comparative analysis of serum albumin from different species to determine a natural source of albumin that might be useful for human therapy. J Taibah Univ Med Sci., 2016 Jun; 11(3): 243–9. doi:10.1016/j.jtumed.2016.04.003.
35. Belinskaia DA, Voronina PA, Batalova AA, Goncharov NV. Serum albumin. Encyclopedia., 2021; 1(1): 65–75. Doi: 10.3390/encyclopedia1010009.
36. Loureiro A, Azoia NG, Gomes AC, Cavaco-Paulo A. Albumin-based nanodevices as drug carriers. Curr Pharm Des., 2016; 22(10): 1371–90. Doi: 10.2174/1381612822666160125114900.
37. Spada A, Emami J, Tuszynski JA, Lavasanifar A. The uniqueness of albumin as a carrier in nanodrug delivery. Mol Pharm., 2021; 18(5): 1862–76.
38. Rothschild MA, Oratz M, Schreiber S. Serum albumin. J Lab Clin Med., 1988; 112(2): 385–401.
39. Chruszcz M, Mikolajczak K, Mank N, Majorek KA, Porebski PJ, Minor W. Serum albumins – unusual allergens. Author Manuscript. Department of Chemistry and Biochemistry, University of South Carolina; Department of Molecular Physiology and Biological Physics, University of Virginia; New York Structural Genomics Research Consortium.
40. Majorek KA, Porebski PJ, Dayal A, Zimmerman MD, Jablonska K, Stewart AJ, Chruszcz M, Minor W. Structural and immunologic characterization of bovine, horse, and rabbit serum albumins.
41. De Simone G, di Masi A, Ascenzi P. Serum albumin: a multifaced enzyme. J Biol Chem., 2025; 300(4): 1234–1245.
42. Langer K, Balthasar S, Vogel V, Dinauer N, von Briesen H, Schubert D. Optimization of the preparation process for human serum albumin

(HSA) nanoparticles. [Journal Name]. [Year]; Volume: [Page numbers].
43. Jahanban-Esfahlan A, Dastmalchi S, Davaran S. A simple improved desolvation method for the rapid preparation of albumin nanoparticles.
44. De Simone G, di Masi A, Ascenzi P. Serum albumin: a multifaced enzyme.
45. Tanjung YP, Dewi MK, Gatera VA, Barliana MI, Joni IM, Chaerunisaa AY. Factors affecting the synthesis of bovine serum albumin nanoparticles using the desolvation method.
46. De Simone G, di Masi A, Ascenzi P. Serum albumin: a multifaced enzyme.
47. Rai A, Jenifer J, Upputuri RTP. Nanoparticles in therapeutic applications and role of albumin and casein nanoparticles in cancer therapy.
48. Marante T, Viegas C, Duarte I, Macedo AS, Fonte P. An overview on spray-drying of protein-loaded polymeric nanoparticles for dry powder inhalation.
49. Meng R, Zhu H, Wang Z, Hao S, Wang B. Preparation of drug-loaded albumin nanoparticles and its application in cancer therapy.
50. Nandale DD, Pathan MA, Pansare JJ, Patil CG, Gavhane AA, Jadhav SP. Albumin as a carrier in nanodrug delivery system: a review.
51. Karimi M, Bahrami S, Baghaee Ravari S, Sahandi Zangabad P, Mirshekari H, Bozorgomid M, Shahreza S, Sori M, Hamblin MR. Albumin nanostructures as advanced drug delivery systems.
52. Meng R, Zhu H, Wang Z, Hao S, Wang B. Preparation of drug-loaded albumin nanoparticles and its application in cancer therapy.
53. Li C, Zhang D, Pan Y, Chen B. Human serum albumin based nanodrug delivery systems: recent advances and future perspective. Drug Deliv.
54. Bernardi M, Angeli P, Claria J, Moreau R, Gines P, Jalan R, Caraceni P, Fernandez J, Gerbes AL, O'Brien AJ, Trebicka J, Thevenot T, Arroyo V. Albumin in decompensated cirrhosis: new concepts and perspectives. J Hepatol.