A Binding Advantage: Optibumin® 25 Demonstrates Enhanced Drug Binding and Consistency Over Plasma Albumin (HSA)

Mark Stathos, PhD, Applications Scientist, Jacob Weber, PhD, Vice President of Process Development, Vladimir Akoyev, PhD, Vice President of Analytical Development, Marcus Curl, Vice President of Product Applications
InVitria, Inc.,USA

APPLICATION BENEFITS

- ***Optibumin 25 supports predictable pharmacokinetics for safer and more consistent dosing***
- ***Streamlines drug formulation by enhancing solubility***
- ***Reduces development risk by eliminating variability from donor-derived raw materials***
- ***Facilitates regulatory compliance through animal-origin-free, cGMP-grade production***
- ***Has no stabilizers and fewer modifications enabling superior drug binding affinity compared to HSA***

INVITRIA SOLUTIONS

Optibumin 25 - Recombinant human serum albumin

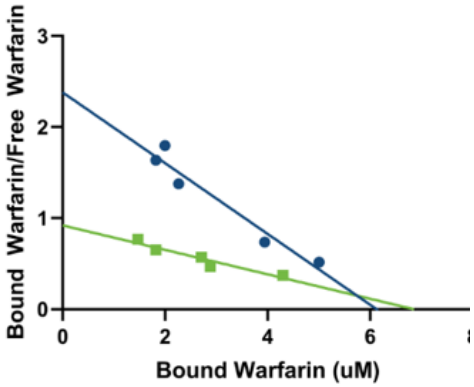


EXECUTIVE SUMMARY

Human serum albumin (HSA) is exemplary among proteins in drug complexation applications. It is capable of binding a wide variety of ligands with high affinity, is resistant to renal filtration, has a lengthy in vivo half-life, is incredibly soluble, and contains multiple drug binding sites. These unique pharmacological properties of albumin are due to its structure, but a protein's structure is complex and heavily influenced by its environment. Because clinical HSA is donor-derived and stabilized with additives, it is heterogeneous and contains aggregates making it suboptimal for high precision applications like drug complexation. To address these shortcomings, InVitria has developed Optibumin 25, a chemically defined, animal-origin-free, excipient-grade, cGMP, recombinant human serum albumin (rHSA). In this application note, we demonstrate that Optibumin 25 has higher binding affinity than HSA for a model drug demonstrating its superiority for precise drug complexation applications.

Key Highlights

- Nearly 3x higher drug-binding affinity vs. plasma HSA
- 10x fewer aggregates ($p < 0.05$)
- 99% reduced Cys34 vs. ~60% in plasma HSA
- No stabilizers that interfere with binding
- Consistent lot-to-lot performance



Optibumin 25 demonstrates threefold higher binding affinity for warfarin compared to plasma HSA ($p < 0.01$).

INTRODUCTION

Albumin is unique among proteins in its ability to bind a plethora of ligands. Classic examples of albumin binding drugs include small molecules such as ibuprofen (Evoli et al., 2017), caffeine (Banipal et al., 2016), and warfarin (O'Reilly, 1967). More recent and innovative examples include the chemotherapeutics Abraxane, [(Desai et al., 2006), (Miele et al 2009), (Green et al 2006)] and Fyarro (Zhou et al 2025), the glucagon like peptide 1 (GLP-1) agonist Semaglutide (Lau et al., 2018) and lipid conjugate siRNAs [(Hoogenboezem et al., 2024), (Sarett et al., 2017), (Colazo et al., 2025)]. Albumin is also a major transporter of important natural bioactive molecules such as lipids, steroid hormones, metal ions and heme (Mishra et al., 2021), (Ashraf et al 2023). Albumin binding to these ligands endows them with many pharmacological benefits.

Complexing with albumin improves drug bioavailability and reduces the need for repeated dosing by improving the in vivo half-life of complexed drugs. There are two main reasons for this benefit. First, with a molecular weight of 66 kDa, albumin and its complex partners are resistant to renal filtration which rapidly clears free molecules smaller than 30-50 kDa (Ruggiero et al., 2010) including peptides, small molecules, and siRNAs. Second, albumin contains a domain that binds the neonatal Fc receptor (FcRn) enabling recycling by the same mechanism that allows long term preservation of IgG in serum (Hoogenboezem and Duvall 2018). This recycling gives both albumin and IgG a remarkable 19-day serum half-life (Liu et al., 2020).

Albumin binding also improves the solubility and reduces the toxicity of its complex partners (Spada et al., 2021). Fatty acids and small molecule drugs are generally hydrophobic and poorly water soluble. Therefore, they are often solubilized in organic solvents like ethanol, DMSO, or DMF but these solvents pose safety risks in vivo (Madsen et al., 2019). Fortunately, albumin has a high binding capacity for these molecules including two main sites for ligand binding termed Sudlow sites I and II (Sudlow et al., 1975) as well as a more generalized site termed simply drug binding site III (Kraugh-Hansen et al., 1983) in addition to seven fatty acid binding sites (Fujiwara et al., 2007). This high binding capacity for ligands obviates the need for toxic solvents.

This amount of hydrophobic cargo would cause many proteins to precipitate, but unlike most proteins, albumin is exceptionally soluble and stable thanks to a globular structure containing 17 disulfide bonds and a strong negative charge at physiological pH (He and Carter, 1992). Albumin's exceptional solubility also enables it to reach very high concentrations in plasma. This allows a substantial reservoir of albumin-bound drug to persist in the plasma and dissociate at a slow controlled rate over time to maintain active free drug concentration over time (Larsen et al., 2016).

Reaping the benefits of albumin drug complexation relies on strong and consistent drug binding which depends on albumin's structure. Unfortunately, serum albumin's structure is intricate and can be influenced by many factors. For example, post-translational modifications (PTMs) such as cysteinylation and glycation are affected by donor age and blood sugar levels respectively (Era et al., 1995), (Rondeau and Bourdon 2011) which can affect drug binding (Lee and Wu, 2015), (Nagumo et al., 2014) as well as FcRn binding (Leblanc et al., 2019), (Ward et al., 2022). Formulation can also impact albumin structure. For instance, the stabilizers sodium octanoate (also known as caprylate or octanoic acid) and N-acetyl tryptophan are added to plasma albumin to stabilize the protein during pasteurization which is required to inactivate bloodborne pathogens. These stabilizers bind to Sudlow site II (Faroongsarng and Kongprasertkit, 2014) which has been shown to interfere with drug binding to the same site (Tramarin et al., 2019), (Kragh-Hansen 1991), (Harm et al., 2018), (Olsen et al., 2004). Aggregation may also impact binding by reducing the surface area available for complexation. All of these factors contribute to pharmacokinetic variation in drug formulation.

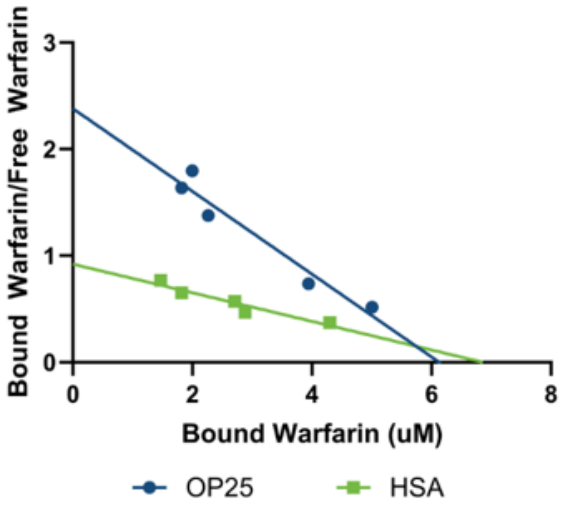
To address these issues, InVitria has developed Optibumin 25, a recombinant, animal-free albumin that is free of stabilizers and aggregates and has few post-translational modifications. Here we compare the binding affinity of Optibumin and plasma HSA for warfarin, a model prescription blood thinning drug that binds to Sudlow site I (Petitpas et al., 2001).

RESULTS AND DISCUSSION

Optibumin 25 has Superior Drug Binding Capacity Compared to HSA

To quantitate the binding affinity of warfarin to Optibumin 25 or HSA, various concentrations of the drug were mixed with constant amounts of either albumin and UV-Vis spectra were recorded to measure total warfarin. Next, free and bound warfarin were separated by low MWCO spin filtration and the retentates and filtrates characterized by UV-Vis to measure bound and free drug respectively.

This data was transformed to create a Scatchard plot (**Figure 1**). Briefly, the Scatchard model assumes that a ligand (e.g. warfarin) and a target (e.g. albumin) each with one binding site interact reversibly to form a complex with a dissociation constant K_D. The plot is a linearized transformation of this relationship where the slope is $-1/K_D$ meaning that a steeper slope is indicative of stronger binding (Scatchard, 1949). Construction of this plot is explained in more detail in the materials and methods.



Albumin	*Slope (-1/KD)*	*Y-Intercept*	*X-Intercept (Bmax)*	*R^2*	*K_D*
Optibumin 25	-0.39	2.38	6.13	0.94	2.58
HSA	-0.13	0.92	6.85	0.92	7.45

Figure 1. *A Scatchard plot showing the binding affinity of Optibumin 25 or HSA for warfarin. Slopes were found to be significantly different by Fisher F-test, $p < 0.01$.*

Because the slope of the Optibumin plot is significantly steeper than that of the HSA plot (Fisher's F-test $p < 0.01$), Optibumin binds warfarin more potently. The measured K_D value of 2.575 µM for Optibumin aligns with the expected 3 µM affinity reported in the literature (Sudlow et al., 1975), (Diana et al., 1989) (Loun and Hage, 1994) whereas the K_D for serum HSA and warfarin, 7.45 µM, was significantly higher indicating that Optibumin binds warfarin exactly as well as predicted whereas HSA exhibits lower than expected binding. Additionally, because the x-intercepts for both regressions are similar, Optibumin and HSA have similar total binding capacities for warfarin.

Importantly, more potent binding would translate to a more significant reservoir effect and a longer in vivo half-life for warfarin in complex with Optibumin versus HSA (Fan et al., 2022). This suggests that Optibumin would retain warfarin for a longer time than serum albumin, causing a more gradual, controlled release of active free drug over time. This means that doses could potentially be raised with less risk of toxicity, or doses could be given less frequently (Dennis et al., 2002). For drugs with a narrow therapeutic index (the ratio of a drug's toxic concentration divided by its effective concentration) such as warfarin (Johnson, 2012) the clinical implications of this could be substantial.

Because warfarin and the stabilizers octanoate and N-acetyl tryptophan all target defined binding sites on albumin, it is expected that they would compete either directly or allosterically for these sites (Yamasaki et al., 1999), (Ghuman et al., 2005). This means that Optibumin, which is uniquely free of these stabilizers (**Table 1**) likely binds to a wide variety of albumin complexing drugs with higher affinity than HSA in addition to warfarin.

Excipient	*Optibumin 25 rHSA*	*Plasma HSA*
Albumin	250 mg/mL	250 mg/mL
Sodium Octanoate	None	16 mM
N-acetyl tryptophan	None	16 mM

Table 1. *Concentrations of common stabilizers in formulations of clinically relevant albumin sources.*

Optibumin 25 Has Fewer Aggregates and Post Translational Modifications Than HSA

Pinpointing the precise mechanism for Optibumin's improved binding affinity is beyond the scope of this work but we offer several hypotheses - which are not mutually exclusive - that could potentially explain this phenomenon. First, it could be that differences in the amount of aggregated albumin present in Optibumin and plasma HSA contribute to this because aggregated albumin has less surface area available to interact with free drug molecules. This hypothesis is supported by our previous observations of differences in aggregation of Optibumin and HSA by capillary electrophoresis (**Figure 2A**). The extent of aggregation from the gel image is quantified in **Figure 2B**. In a sample of 3 lots of Optibumin and 5 lots of HSA, we found that Optibumin had a mean of 39000 area units per µg of protein compared to 403000 area units per µg of protein for HSA, an astounding 10-fold difference that was statistically significant (Welch's t test $p < 0.05$). Furthermore, Optibumin had a standard deviation of 11000 area units per µg of protein while HSA had a standard deviation of 257000 area units per µg of protein which was also a significant difference (F test for variance, $p < 0.01$). This demonstrates that Optibumin is more consistent than clinical HSA which is paramount when trying to adjust dosing regimens of drugs with a narrow therapeutic window to maintain efficacy and avoid toxicity (Celestin et al., 2022).

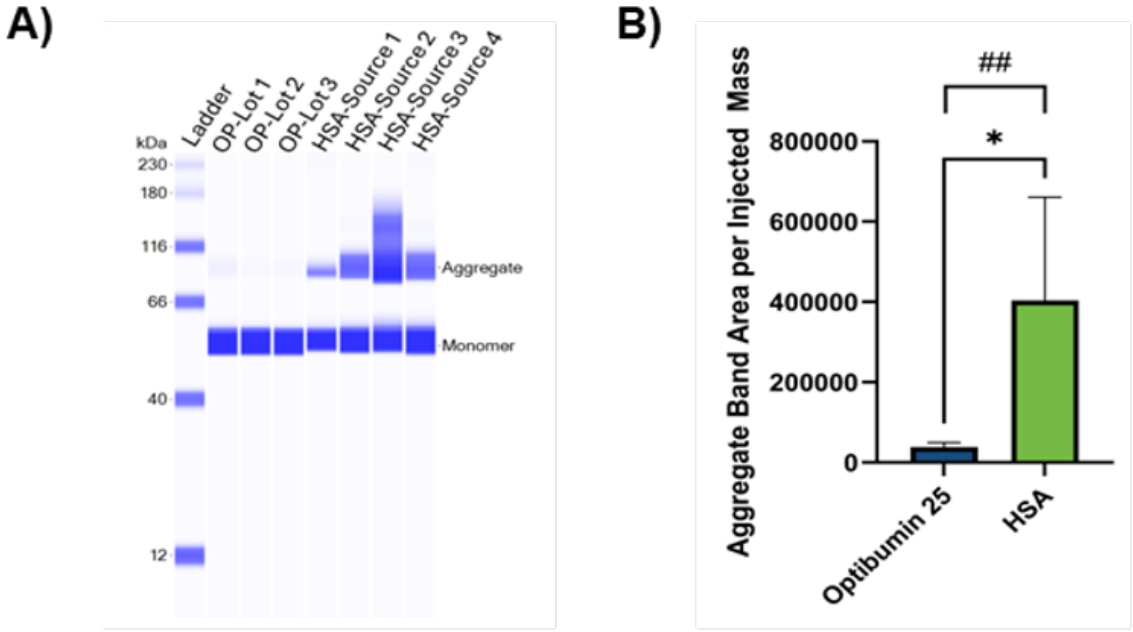


Figure 2. *Characterization of aggregation in Optibumin and HSA. A) Capillary Electrophoresis images of samples from 3 different lots of Optibumin and 4 different lots of HSA. The first lane is the molecular weight marker, lanes 2-8 are samples prepared at an albumin concentration of 0.5 mg/mL. B) Quantitative comparison of the extent of aggregation of Optibumin and HSA from the gel image in terms of aggregate band area per injected mass (* = p <0.05 Welch's t test for differences in mean) (## = p < 0.01 F-test for differences in variance).*

Second, it could be that bound stabilizers or post translational modifications on plasma albumin interfere with the drug interaction. The presence of stabilizers has been directly linked to reduced ligand binding capacity (Park et al., 2021). As an example of the effect of posttranslational modifications on binding, cysteinylation of albumin's lone free cysteine, Cys34, has been implicated in reducing warfarin binding (Nagumo et al., 2014). We have previously shown that plasma HSA is 40% cysteinylated whereas Optibumin is 99% unmodified at this residue (**Figure 3**) and observed significant differences in both mean and variance of cysteinylation between Optibumin and plasma HSA. This superior consistency can help improve predictability in the clinic which could lead to better outcomes (Fender et al., 2019). Fatty acid binding or other post translational modifications such as glycation can also contribute to this effect (Vorum et al., 1993). Furthermore, in some cases ligands that bind to one Sudlow site such as octanoate, can allosterically affect binding to the other Sudlow site (Yamasaki et al., 1999), (Ghuman et al., 2005).

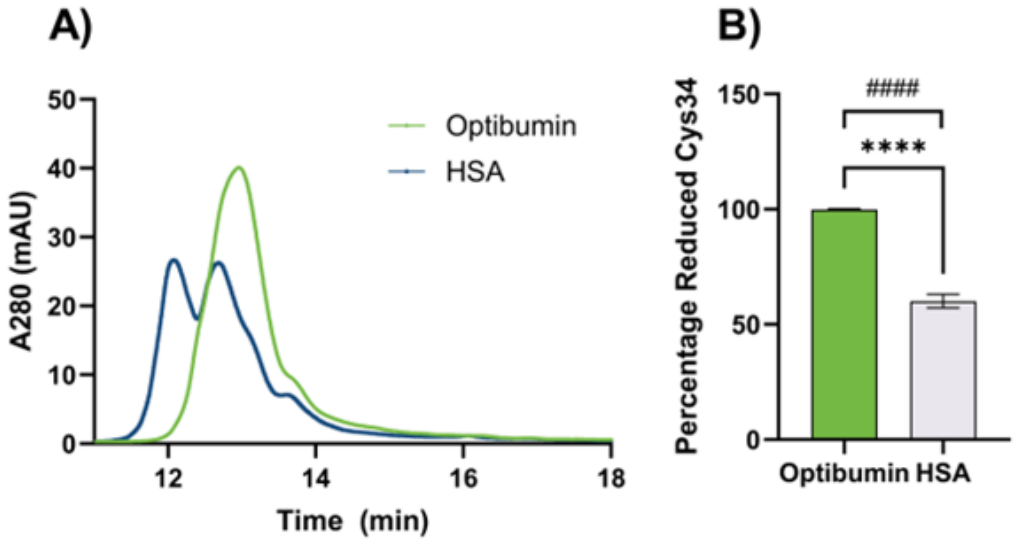


Figure 3. *Analytical Characterization of Cys34 Redox State of Optibumin and HSA by HPLC. Figure 3A, representative chromatograms of Optibumin (green) and plasma HSA (blue). Figure 3B, Mean percentage of reduced Cys34 in 9 lots of plasma albumin and 10 lots of Optibumin 25 **** $p < 0.0001$ Welch's unpaired t test for differences in mean #### $p < 0.0001$ F-test for differences in variance.*

MATERIALS & METHODS

Warfarin Standard Curve Development

Warfarin sodium salt was prepared at a stock concentration of 1 mg/mL in deionized water. The stock was then serially diluted 2-fold to get concentrations spanning 4 orders of magnitude. The UV-Vis absorbance spectrum was recorded for each sample to generate a standard curve and define the linear range of the absorbance at the spectral peak of 310 nm to enable quantitation of free warfarin.

Albumin Preparation

Plasma HSA was desalted by spin filtration to remove N-acetyl tryptophan which interferes with absorbance measurements at 280 nm. This was not necessary for Optibumin because it contains no such additives. Stocks of Optibumin and HSA were prepared at 0.2 mg/ml as measured by A_{280} were prepared for complexing reactions.

Albumin-Drug Complexing

To evaluate the binding affinity of albumin to warfarin, Optibumin or HSA were first mixed 1:1 with serial dilutions of warfarin. These dilutions spanned the pre-established linear range of warfarin concentrations detectable by UV-Vis for a final albumin concentration of 0.1 mg/mL and a final sample volume of 1 mL. The absorbance spectra of the samples were then recorded. This represented the total warfarin (free and bound together). The samples were then buffer exchanged by spin filtration through a 3 kDa MWCO membrane. The flowthrough and retentate were each adjusted to total volumes of 1 mL each and quantified by UV-Vis. The flowthrough comprised free warfarin and the retentate comprised bound warfarin. The contribution of albumin to the total and bound warfarin was subtracted.

Scatchard Plot Construction and Interpretation

The strength of binding of a drug to a target is defined as $K_D = k_{off}/k_{on}$ where k_{off} and k_{on} are the kinetic rate constants governing dissociation and association of the drug to the target respectively. The lower the K_D, the less dissociation and the stronger the binding affinity. Drug binding can be plotted as the proportion of total drug that is bound, on the y-axis vs free drug on the x-axis to get an isothermal binding curve (Weber et al., 2020). On these plots, K_D is the point on the x-axis where the y value is half its maximum. However, because these plots are nonlinear, interpretation can be challenging, and accurate fitting requires many data points. The Scatchard plot addresses these issues by linearizing the relationship between the drug

and target concentrations. This transformation is relatively straightforward and given below.

The Scatchard model relies on reversible association and dissociation of a free drug D and unbound target T to form a drug target complex DT

$$[D]+[T]\underset{k_{off}}{\overset{k_{on}}{\rightleftharpoons}}\left[DT\right]$$

According to the law of mass action, the rate of reaction depends on the kinetic rate constants and the concentrations of reactants. If we assume the reaction is at equilibrium i.e. association and dissociation occur at the same rate, then we have:

$$k_{on}[D][T]= k_{off}[DT]$$

Using the definition of K_D we have:

$$K_D = \frac{k_{off}}{k_{on}} = \frac{[D][T]}{[DT]}$$

Let n_{bar} be the average number of sites on the target bound by the drug and let T_{total} be the total number of target sites

$$\overline{n} = \frac{[DT]}{[T]_{total}} = \frac{[DT]}{[T]+[DT]}$$

Solving for the concentration of free target sites:

$$[T]= [T]_{total} -[DT]= [T]_{total}(1-\overline{n})$$

Rearranging the equation for KD by substituting n_{bar}

$$K_D = \frac{(1-\overline{n})[T]_{total}[D]}{\overline{n}[T]_{total}} = \frac{(1-\overline{n})[D]}{\overline{n}}$$

Rearranging further to solve for n_{bar} /D:

$$\frac{\overline{n}}{[D]} = \frac{1-\overline{n}}{K_D} = \frac{1}{K_D} - \frac{\overline{n}}{K_D}$$

This is the Scatchard equation in which n_{bar}/D, the ratio of bound to free drug is on the y-axis, n_{bar} the proportion of drug that is bound, is on the x-axis, $-1/K_D$ is the y-intercept and $-n/K_D$ is the slope. While the axes may not be immediately intuitive, the advantage is that K_D, the most critical parameter for drug binding, can easily be determined from the slope of the plot.

Aggregate Analysis

Liquid samples of Optibumin 25 and HSA were diluted down to 1 mg/mL and 0.5 mg/mL using 20 mM phosphate buffer, 50mM NaCl, pH 7. For the powdered sources, HSA source 3 and source 4, samples were reconstituted initially at 5-10 mg/mL and diluted down to 1 and 0.5 mg/mL using 20 mM phosphate buffer, 50 mM NaCl, pH 7. These diluted samples were subsequently used for quantifying albumin aggregate using chemiluminescence-based capillary electrophoresis on a Wes system (ProteinSimple, San Jose, CA). Samples were prepared under native conditions by reconstituting the fluorescent master mix supplied by ProteinSimple in water only (no DTT or SDS sample buffer were added) and mixing with the albumin samples at a 1 to 5 ratio (1 part fluorescent master mix and 5 parts diluted albumin samples). Albumin aggregate was analyzed using the Compass for SW software (version 6.3.0). The aggregate area (any detection above the main monomer band at ~60 kDa) was quantified using dropped line peak analysis. For each sample, the total aggregate area was divided by the diluted concentration, either 1 mg/mL or 0.5 mg/mL, to obtain the “aggregate band area per injected mass.” Statistical analysis was run to show that aggregate area was significantly lower for Optibumin (Welch’s t test) and more consistent lot to lot than HSA (f test for equality of variance).

CONCLUSION

InVitria’s Optibumin 25 recombinant albumin was shown to have a higher affinity than HSA for the model albumin binding drug warfarin. This improved binding could have important pharmacological benefits such as enabling lower or less frequent drug dosing or improving safety and efficacy. It is likely this improved binding is due to differences in: formulation (i.e. the presence of stabilizers in HSA but not Optibumin), post-translational modifications (the presence of cysteinylated albumin in HSA but not Optibumin), and/or aggregation which was significantly lower in Optibumin than HSA. Furthermore, Optibumin also demonstrated more consistency in aggregation and oxidation state, suggesting that complexing drug to Optibumin could improve pharmacokinetics, which could have clinical benefits. Taken together, these factors along with its recombinant animal-origin-free nature, make Optibumin 25 the superior albumin for drug complexation applications.

REFERENCES

Ashraf, S., Qaiser, H., Tariq, S., Khalid, A., Makeen, H. A., Alhazmi, H. A., & Ul-Haq, Z. (2023). Unraveling the versatility of human serum albumin: A comprehensive review of its biological significance and therapeutic potential. Current Research in Structural Biology, 6, 100114. https://doi.org/10.1016/j.crstbi.2023.100114

Banipal, T. S., Kaur, N., & Banipal, P. K. (2016). Binding studies of caffeine and theophylline to bovine serum albumin: Calorimetric and spectroscopic approach. Journal of Molecular Liquids, 223, 1048–1055. https://doi.org/10.1016/j.molliq.2016.09.034

Celestin, M. N., & Musteata, F. M. (2021). Impact of changes in free concentrations and drug–protein binding on drug dosing regimens in special populations and disease states. Journal of Pharmaceutical Sciences, 110(10), 3331–3344. https://doi.org/10.1016/j.xphs.2021.05.018

Colazo, J. M., Keech, M. C., Shah, V., Hoogenboezem, E. N., Lo, J. H., Francini, N., Cassidy, N. T., Yu, F., Sorets, A. G., McCune, J. T., DeJulius, C. R., Cho, H., Michell, D. L., Maerz, T., Vickers, K. C., Gibson-Corley, K. N., Hasty, K. A., Crofford, L. J., Cook, R. S., & Duvall, C. L. (2025). siRNA conjugate with high albumin affinity and degradation resistance for delivery and treatment of arthritis in mice and guinea pigs. Nature Biomedical Engineering, 9, 1366–1383. https://doi.org/10.1038/s41551-025-00945-1

Dennis, M. S., Zhang, M., Meng, Y. G., Kadkhodayan, M., Kirchhofer, D., Combs, D., & Damico, L. A. (2002). Albumin binding as a general strategy for improving the pharmacokinetics of proteins. Journal of Biological Chemistry, 277(38), 35035–35043. https://doi.org/10.1074/jbc.M205854200

Desai, N., Trieu, V., Yao, Z., Louie, L., Ci, S., Yang, A., Tao, C., De, T., Beals, B., Dykes, D., Noker, P., Yao, R., Labao, E., Hawkins, M., & Soon-Shiong, P. (2006). Increased antitumor activity, intratumor paclitaxel concentrations, and endothelial cell transport of cremophor-free, albumin-bound paclitaxel (ABI-007), compared with cremophor-based paclitaxel. Clinical Cancer Research, 12(4), 1317–1324. https://doi.org/10.1158/1078-0432.CCR-05-1634

Diana, F. J., Veronich, K., & Kapoor, A. L. (1989). Binding of nonsteroidal anti-inflammatory agents and their effect on binding of racemic warfarin and its enantiomers to human serum albumin. Journal of Pharmaceutical Sciences, 78(3), 195–199. https://doi.org/10.1002/jps.2600780304

Evoli, S., Mobley, D. L., Guzzi, R., & Rizzuti, B. (2016). Multiple binding modes of ibuprofen in human serum albumin identified by absolute binding free energy calculations. Physical Chemistry Chemical Physics, 18(47), 32358–32368. https://doi.org/10.1039/c6cp05680f

Era, S., Kuwata, K., Imai, H., Nakamura, K., Hayashi, T., & Sogami, M. (1995). Age-related change in redox state of human serum albumin. Biochimica et Biophysica Acta (BBA) - Protein Structure and Molecular Enzymology, 1247(1), 12–16. https://doi.org/10.1016/0167-4838(94)00166-E

Fan, J., Gilmartin, K., Octaviano, S., Villar, F., Remache, B., & Regan, J. (2022). Using human serum albumin binding affinities as a proactive strategy to affect the pharmacodynamics and pharmacokinetics of preclinical drug candidates. ACS Pharmacology & Translational Science, 5(9), 803–810. https://doi.org/10.1021/acsptsci.2c00115

Fender, A. C., & Dobrev, D. (2019). Bound to bleed: How altered albumin binding may dictate warfarin treatment outcome. International Journal of Cardiology: Heart & Vasculature, 22, 214–215. https://doi.org/10.1016/j.ijcha.2019.02.007

Fischer, N. H., Lopes van den Broek, S. I., Herth, M. M., & Diness, F. (2022). Radiolabeled albumin through SNAr of cysteines as a potential pretargeting theranostic agent. RSC Advances, 12, 35032–35036. https://doi.org/10.1039/D2RA06406E

Fujiwara, S., & Amisaki, T. (2007). Identification of high-affinity fatty acid binding sites on human serum albumin by the MM-PB-SA method. Biophysical Journal, 94(1), 95–103. https://doi.org/10.1529/biophysj.107.111377

Ghuman, J., Zunszain, P. A., Petitpas, I., Bhattacharya, A. A., Otagiri, M., & Curry, S. (2005). Structural basis of the drug-binding specificity of human serum albumin. Journal of Molecular Biology, 353(1), 38–52. https://doi.org/10.1016/j.jmb.2005.07.075

Gong, J., Yan, J., Forscher, C., & Hendifar, A. (2018). Aldoxorubicin: A tumor-targeted doxorubicin conjugate for relapsed or refractory soft tissue sarcomas. Drug Design, Development and Therapy, 12, 777–786. https://doi.org/10.2147/DDDT.S140638

Green, M. R., Manikhas, G. M., Orlov, S., Afanasyev, B., Makhson, A. M., Bhar, P., & Hawkins, M. J. (2006). Abraxane, a novel cremophor-free, albumin-bound particle form of paclitaxel for the treatment of advanced non-small-cell lung cancer. Annals of Oncology, 17(8), 1263–1268. https://doi.org/10.1093/annonc/mdl104

Harm, S., Schildböck, C., & Hartmann, J. (2018). Removal of stabilizers from human serum albumin by adsorbents and dialysis used in blood purification. PLoS ONE, 13(1), e0191741. https://doi.org/10.1371/journal.pone.0191741

He, X. M., & Carter, D. C. (1992). Atomic structure and chemistry of human serum albumin. Nature, 358(6383), 209–215. https://doi.org/10.1038/358209a0

Hoogenboezem, E. N., Patel, S. S., Lo, J. H., Cavnar, A. B., Babb, L. M., Francini, N., … Duvall, C. L. (2024). Structural optimization of siRNA conjugates for albumin binding achieves effective MCL1-targeted cancer therapy. Nature Communications, 15(1), 1581. https://doi.org/10.1038/s41467-024-45609-0

Hoogenboezem, E. N., & Duvall, C. L. (2018). Harnessing albumin as a carrier for cancer therapies. Advanced Drug Delivery Reviews, 130, 73–89. https://doi.org/10.1016/j.addr.2018.07.011

Johnson, J. A. (2012). Warfarin pharmacogenetics: A rising tide for its clinical value. Circulation, 125(16), 1964–1966. https://doi.org/10.1161/CIRCULATIONAHA.112.100628

Kragh-Hansen, U. (1983). Relations between high-affinity binding sites for L-tryptophan, diazepam, salicylate, and phenol red on human serum albumin. Biochemical Journal, 209(1), 135–142. https://doi.org/10.1042/bj2090135

Kragh-Hansen, U. (1991). Octanoate binding to the indole- and benzodiazepine-binding region of human serum albumin. Biochemical Journal, 273(3), 641–644. https://doi.org/10.1042/bj2730641

Larsen, M. T., Kuhlmann, M., Hvam, M. L., & Howard, K. A. (2016). Albumin-based drug delivery: Harnessing nature to cure disease. Molecular and Cellular Therapies, 4, 3. https://doi.org/10.1186/s40591-016-0048-8

Lau, J., Bloch, P., Schäffer, L., Pettersson, I., Spetzler, J., Kofoed, J., … Kruse, T. (2015). Discovery of the once-weekly glucagon-like peptide 1 (GLP-1) analogue semaglutide. Journal of Medicinal Chemistry, 58(18), 7370–7380. https://doi.org/10.1021/acs.jmedchem.5b00726

Leblanc, Y., Berger, M., Seifert, A., Bihoreau, N., & Chevreux, G. (2019). Human serum albumin presents isoform variants with altered neonatal Fc receptor interactions. Protein Science, 28(11), 1982–1992. https://doi.org/10.1002/pro.3733

Lee, P., & Wu, X. (2015). Modifications of human serum albumin and their binding effect. Current Pharmaceutical Design, 21(14), 1862–1865. https://doi.org/10.2174/1381612821666150302115025

Liu, X., Mohanty, R. P., Maier, E. Y., Peng, X., Wulfe, S., Looney, A. P., Aung, K. L., & Ghosh, D. (2020). Controlled loading of albumin–drug conjugates ex vivo for enhanced drug delivery and antitumor efficacy. Journal of Controlled Release, 328, 1–12. https://doi.org/10.1016/j.jconrel.2020.08.015

Loun, B., & Hage, D. S. (1994). Chiral separation mechanisms in protein-based HPLC columns. 1. Thermodynamic studies of (R)- and (S)-warfarin binding to immobilized human serum albumin. Analytical Chemistry, 66(21), 3814–3822. https://doi.org/10.1021/ac00093a043

Madsen, B. K., Hilscher, M., Zetner, D., & Rosenberg, J. (2019). Adverse reactions of dimethyl sulfoxide in humans: A systematic review. F1000Research, 7, 1746. https://doi.org/10.12688/f1000research.16642.2

Mehtala, J. G., Kulczar, C., Lavan, M., Knipp, G., & Wei, A. (2015). Cys34-PEGylated human serum albumin for drug binding and delivery. Bioconjugate Chemistry, 26(5), 941–949. https://doi.org/10.1021/acs.bioconjchem.5b00143

Miele, E., Spinelli, G. P., Miele, E., Tomao, F., & Tomao, S. (2009). Albumin-bound formulation of paclitaxel (Abraxane® ABI-007) in the treatment of breast cancer. International Journal of Nanomedicine, 4, 99–105. https://doi.org/10.2147/ijn.s3061

Mishra, V., & Heath, R. J. (2021). Structural and biochemical features of human serum albumin essential for eukaryotic cell culture. International Journal of Molecular Sciences, 22(16), 8411. https://doi.org/10.3390/ijms22168411

Nagumo, K., Tanaka, M., Chuang, V. T. G., Setoyama, H., Watanabe, H., Yamada, N., Kubota, K., Tanaka, M., Matsushita, K., Yoshida, A., Jinnouchi, H., Anraku, M., Kadowaki, D., Ishima, Y., Sasaki, Y., Otagiri, M., & Maruyama, T. (2014). Cys34-cysteinylated human serum albumin is a sensitive plasma marker in oxidative stress-related chronic diseases. PLoS ONE, 9(1), e85216. https://doi.org/10.1371/journal.pone.0085216

Oettl, K., & Marsche, G. (2010). Redox state of human serum albumin in terms of cysteine-34 in health and disease. In Methods in Enzymology (Vol. 474, pp. 181–195). Academic Press. https://doi.org/10.1016/S0076-6879(10)74011-8

Olsen, H., Andersen, A., Nordbø, A., Kongsgaard, U. E., & Børmer, O. P. (2004). Pharmaceutical-grade albumin: Impaired drug-binding capacity in vitro. BMC Clinical Pharmacology, 4, 4. https://doi.org/10.1186/1472-6904-4-4

O'Reilly, R. A. (1967). Studies on the coumarin anticoagulant drugs: Interaction of human plasma albumin and warfarin sodium. The Journal of Clinical Investigation, 46(5), 829–837. https://doi.org/10.1172/JCI105582

Park, J. H., Lee, J. W., Kang, K., & Bae, S. H. (2021). Effect of stabilizers on drug binding capacity of human serum albumin. Pharmaceuticals, 14(12), 1295. https://doi.org/10.3390/ph14121295

Petitpas, I., Bhattacharya, A. A., Twine, S., East, M., & Curry, S. (2001). Crystal structure analysis of warfarin binding to human serum albumin: Anatomy of drug site I. Journal of Biological Chemistry, 276(25), 22804–22809. https://doi.org/10.1074/jbc.M100575200

Rondeau, P., & Bourdon, E. (2011). The glycation of albumin: Structural and functional impacts. Biochimie, 93(4), 645–658. https://doi.org/10.1016/j.biochi.2010.12.003

Ruggiero, A., Villa, C. H., Bander, E., Rey, D. A., Bergkvist, M., Batt, C. A., Manova-Todorova, K., Deen, W. M., Scheinberg, D. A., & McDevitt, M. R. (2010). Paradoxical glomerular filtration of carbon nanotubes. Proceedings of the National Academy of Sciences, 107(27), 12369–12374. https://doi.org/10.1073/pnas.0913667107

Sand, K. M. K., Bern, M., Nilsen, J., Noordzij, H. T., Sandlie, I., & Andersen, J. T. (2015). Unraveling the interaction between FcRn and albumin: Opportunities for design of albumin-based therapeutics. Frontiers in Immunology, 5, 682. https://doi.org/10.3389/fimmu.2014.00682

Sarett, S. M., Werfel, T. A., Lee, L., Jackson, M. A., Kilchrist, K. V., Brantley-Sieders, D., & Duvall, C. L. (2017). Lipophilic siRNA targets albumin in situ and promotes bioavailability, tumor penetration, and carrier-free gene silencing. Proceedings of the National Academy of Sciences, 114(32), E6490–E6497. https://doi.org/10.1073/pnas.1621240114

Scatchard, G. (1949). The attractions of proteins for small molecules and ions. Annals of the New York Academy of Sciences, 51(4), 660–672. https://doi.org/10.1111/j.1749-6632.1949.tb27297.x

Spada, A., Emami, J., Tuszynski, J. A., & Lavasanifar, A. (2021). The uniqueness of albumin as a carrier in nanodrug delivery. Molecular Pharmaceutics, 18(5), 1866–1883. https://doi.org/10.1021/acs.molpharmaceut.1c00090

Sudlow, G., Birkett, D. J., & Wade, D. N. (1975). The characterization of two specific drug-binding sites on human serum albumin. Molecular Pharmacology, 11(6), 824–832. https://pubmed.ncbi.nlm.nih.gov/1207674/

Tramarin, A., Tedesco, D., Naldi, M., Baldassarre, M., Bertucci, C., & Bartolini, M. (2019). New insights into the altered binding capacity of pharmaceutical-grade human serum albumin: Site-specific binding studies by induced circular dichroism spectroscopy. Journal of Pharmaceutical and Biomedical Analysis, 162, 171–178. https://doi.org/10.1016/j.jpba.2018.09.022

Vorum, H., Jørgensen, H. R., & Brodersen, R. (1993). Variation in the binding affinity of warfarin and phenprocoumon to human serum albumin in relation to surgery. European Journal of Clinical Pharmacology, 44(2), 157–162. https://doi.org/10.1007/BF00315474

Ward, E. S., Gelinas, D., Dreesen, E., Van Santbergen, J., Andersen, J. T., Silvestri, N. J., Kiss, J. E., Sleep, D., Rader, D. J., Kastelein, J. J. P., Louagie, E., Vidarsson, G., & Spriet, I. (2022). Clinical significance of serum albumin and implications of FcRn inhibitor treatment in IgG-mediated autoimmune disorders. Frontiers in Immunology, 13, 892534. https://doi.org/10.3389/fimmu.2022.892534

Weber, J. J., Kanost, M. R., & Gorman, M. J. (2020). Iron binding and release properties of transferrin-1 from Drosophila melanogaster and Manduca sexta: Implications for insect iron homeostasis. Insect Biochemistry and Molecular Biology, 125, 103438. https://doi.org/10.1016/j.ibmb.2020.103438

Yamasaki, K., Maruyama, T., Yoshimoto, K., Tsutsumi, Y., Narazaki, R., Fukuhara, A., Kragh-Hansen, U., & Otagiri, M. (1999). Interactive binding to the two principal ligand-binding sites of human serum albumin: Effect of the neutral-to-base transition. Biochimica et Biophysica Acta (BBA) - Protein Structure and Molecular Enzymology, 1432(2), 313–323. https://doi.org/10.1016/S0167-4838(99)00098-9

Yu, L., Hua, Z., Luo, X., Zhao, T., & Liu, Y. (2022). Systematic interaction of plasma albumin with the efficacy of chemotherapeutic drugs. Biochimica et Biophysica Acta (BBA) - Reviews on Cancer, 1877(1), 188655. https://doi.org/10.1016/j.bbcan.2021.188655

Zhang, Y., Jia, Y., & Zhu, S. (2023). NIR-II cyanine@albumin fluorophore for deep tissue imaging and imaging-guided surgery. SmartMat, 4(1), e1245. https://doi.org/10.1002/smm2.1245

Zhou, R., Zhong, R., Luo, Z., Wei, H., & Yu, C.-Y. (2025). Advances on albumin-based carriers for anticancer drug delivery. Advanced NanoBiomed Research, 5(9), 2500011. https://doi.org/10.1002/anbr.202500011

ORDERING INFORMATION

Optibumin 25 - Recombinant Human Serum Albumin (25% Solution) Animal-Origin-Free | GMP-Produced	555HSA0075
Optibumin 25 - Recombinant Human Serum Albumin, 100 mL Bags	555HSA0075-100mL-BG
Optibumin 25 - Recombinant Human Serum Albumin, 100 mL Bottles	555HSA0075-100mL-BT

ABOUT INVITRIA

InVitria is a global leader in developing and manufacturing high-performance, animal-origin-free cell culture supplements and recombinant proteins. Our products eliminate human and animal serum-derived components to improve consistency, reduce regulatory burden, and accelerate the approval of life-changing therapies. Trusted in clinical and commercial production of cell and gene therapies, vaccines, regenerative medicine, and medical devices, InVitria supports cGMP and ISO-compliant manufacturing aligned with FDA and EMA expectations. Scalable to meet growing global demand, our chemically defined solutions enable safer, more efficient biomanufacturing.

InVitria
Performance. Defined.

Copyright © 2025 InVitria, Inc. All rights reserved.
Reproduction or distribution of any InVitria materials, in whole or in part, is prohibited without prior written consent. All logos, names, designs, and marks displayed, including InVitria®, the InVitria brand design and Optibumin®, are trademarks or service marks owned or licensed by InVitria, Inc., Kansas, USA, unless otherwise noted. ProteinSimple® is a registered trademark of ProteinSimple, a Bio-Techne brand. For details on InVitria's registered intellectual property, patents, and additional terms and conditions, please visit www.InVitria.com/terms.

InVitria, Inc.
2718 Industrial Drive
Junction City, KS 66441 USA
Phone: 800-916-8311
Fax: 785-238-5688
Email: info@invitria.com
www.invitria.com