

MedNut Mail

The How, What, Which, Where, When and Why of pharmaconutrition



About albumin

Y Coleman

18th March 2025

<https://medicationsandnutrition.com/mednut-mail/>

Editorial

Albumin aka Human Serum Albumin (HSA) is the main protein in the blood. It is part of a superfamily that includes vitamin D-binding protein (VDBP), alpha-fetoprotein and alpha-2-macroglobulin (afamin). [Recent seminal research](https://doi.org/10.1186/s12967-024-05000-5) (DOI <https://doi.org/10.1186/s12967-024-05000-5>) has also identified albumin as a glycoprotein.

Because albumin is their primary distribution carrier, how compounds interact with albumin determines compound half-life, absorption, distribution, metabolism, and excretion.

Both albumin and the membrane transporters are commonly referred to as transporters. To minimise confusion, I shall refer to blood-specific distribution vehicles as carriers.

Functions

Albumin's range of functions is extensive and includes -

- modulator of plasma oncotic pressure (the pressure exerted by plasma proteins on capillary walls), osmotic pressure, and pH;
- endothelial stabilization, immune regulation, enzyme activities, and anti-oxidant properties;
- carrier of endogenous compounds including water, bilirubin, fatty acids, nutrients;
- carrier of exogenous compounds including metals, toxins, pharmaceuticals;
- biomarker of -
 - oxidative stress;
 - diseases such as cancer, rheumatoid arthritis, diabetes;
 - nutritional status, and a predictor of the outcome of many pathologies.

In some disease states, albumin can -

- be reduced in quantity and quality. The concept of 'effective albumin concentration' refers to the amount of albumin that is structurally and functionally intact;
- have normal quantity, and altered function;

About albumin

- be sufficiently modified that its binding properties and function are significantly affected to alter physiological responses.

Synthesis

Albumin's key statistics –

- typically takes about 15-30 minutes to produce,
- rate of synthesis that depends on amino acid supply, especially tryptophan, and is also affected by nutritional status and oncotic pressure,
- circulatory half-life is 16 hours,
- continuous secretion into the bloodstream,
- healthy adults produce 10–15 g of albumin per day,
- typical healthy adult range is 35-50 g/L.

Hypoalbuminaemia

Hypoalbuminaemia occurs when there is both reduced synthesis and increased catabolism.

Factors causing hypoalbuminaemia include fasting, poor nutritional status, high osmotic pressure, and inflammation eg tumor necrosis factor α (TNF α), interleukin-6 (IL-6).

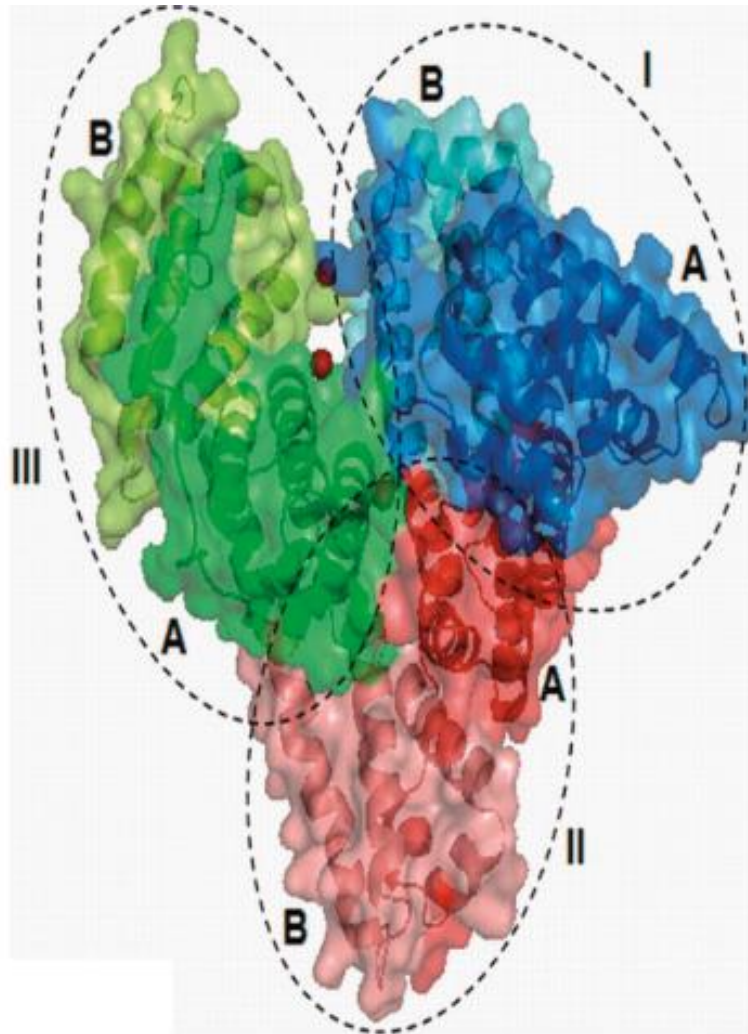
Albumin structure

The albumin structure is a single chain polypeptide (amino acids) chain. It comprises 3 domains (I, II, III), and each domain contains 2 subdomains (A, B). There is minimal contact between domains I + III, and all primary contact is through domain II. The subdomains contain a variety of amino acid-based binding sites.

The structure is very open and vaguely based on a heart or V shape. An open structure means it can carry compounds with a variety of shapes and sizes. A range of factors, endogenous and/or exogenous, can alter albumin's structure, resulting in altered functionality and effectiveness. The ultimate outcomes of modification to albumin's structure are both altered metabolic processes, and altered therapeutic benefit of interventions.

About albumin

Some analogies about albumin. Albumin has size constraints like a cargo plane and cannot add extra trailers like a road train. It has defined zoned areas with limited overlap like a cargo boat (wheelhouse, kitchen/galley, crew quarters, engine room, cargo). Its route is defined similarly to a train.



Structure of human serum albumin representing 3 domains (I, II, and III) and their 2 subdomains (A and B).

From - [At very low concentrations known chaotropes act as kosmotropes for the N and B isoforms of human serum albumin](https://doi.org/10.1139/bcb-2012-0035) .
<https://doi.org/10.1139/bcb-2012-0035>

Binding sites

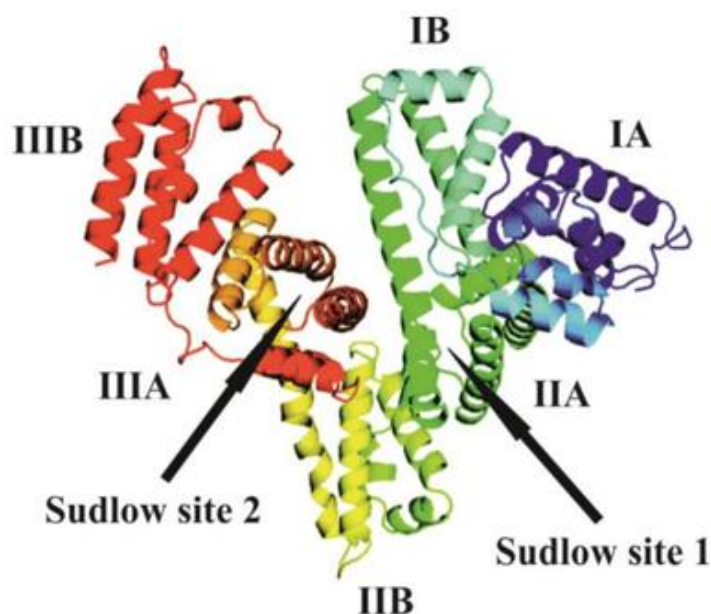
The albumin structure is designed to accommodate multiple binding sites and with some flexibility for compound shape and size.

Binding between compounds and albumin is determined by the number and availability of binding sites for each compound, and albumin's affinity for the compound.

About albumin

Identified binding sites include -

1. **Sudlow site I.** Is located in subdomain IIA. Compounds include bulky heterocyclic molecules such as dicarboxylic acids. Site I shows poor stereoselectivity, which might also be due to the flexibility of this site.
2. **Sudlow site II.** Aka FA3-4 site, and is located in subdomain IIIA. Compounds include aromatic carboxylates with an extended conformation. Site II often shows stereoselectivity and therefore is less flexible.
3. **Binding site 3.** Aka FA1 site and is located in subdomain IB.
4. **FA5 site.** Located in subdomain IIIB.
5. **Subdomains IA + IIB.** The evidence is sparse to non-existent with regard to any compounds associated with these subdomains.



[Unleashing Untargeted Hyphenated Ms Analysis With Chemometrics - Scientific Figure on ResearchGate.](https://www.researchgate.net/figure/The-structure-of-human-serum-albumin-fig32_315894461)
Available from: https://www.researchgate.net/figure/The-structure-of-human-serum-albumin-fig32_315894461

There seem to be 3 key areas for albumin-based drug-nutrient interactions –

- a) structural changes altering access to binding sites, especially nutrient access.
Note - drug-induced structural changes impacting drug effects are much more likely to be investigated and known;
- b) competition between drugs and nutrients for shared binding sites;
- c) inhibited access to the carrier. A known example is aspirin's inhibition of vitamin C access to albumin ([MedNut Mail Aspirin-vitamin C interactions](#)).

I have allocated these mostly unknown, key interactions to the “why don’t we know this already” basket.

Clinical Concerns

The “salting” of drugs with nutrients to utilise albumin as their distribution vehicle is a potential source of nutrient toxicity. Consequently, nutrient content in each drug dose should be included in the Product Information documents. As these are “new” techniques, the Regulators are yet to initiate any decrees – let’s hope they do so and soon.

There is no regulatory requirement for Product Information documents to include –

- the impacts of pharmaceuticals and nutrients the albumin structure,
- the specific subdomains and their specific binding sites for each pharmaceutical product.

Clinical Questions

What actions will you initiate as you review a person whose prescribed medications profile includes one or more drugs that utilize albumin as a carrier, will you -

- recommend checking inflammatory markers such as TNF- α and IL-6, and B12 status (because it also impacts TNF- α status) if hypoalbuminaemic?

Conclusions

Albumin is the primary carrier in the body’s distribution system. The evidence for albumin-based drug-nutrient interactions is remarkably limited.

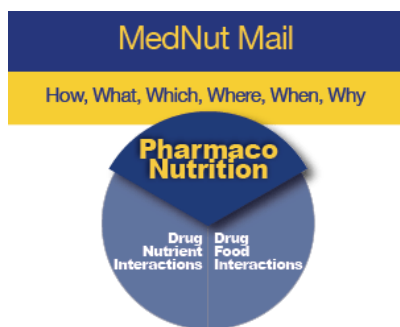
About albumin

Please read this as it is important ...

The information in this article is provided to support Health Professionals. It is not an exhaustive protocol and Health Professionals are advised that adequate professional supervision is accessed to ensure that Duty of Care obligations with respect to safe administration of medicines is met for each consumer.

Medications have profoundly and positively changed health outcomes however they do generally come with some nutritional harms. By identifying and addressing the nutritional harms, optimal health outcomes are closer to being achieved.

You may be interested in some of our other products ...



MedNut Mail is our free weeklyish email that identifies and comments upon various aspects of pharmaconutrition.

[For more information click here.](#)



For innovative clinicians wanting to include drug-nutrition interactions into their daily clinical practice in order to optimise outcomes for those in their care.

[For more information click here.](#)

Connect with us on

