

MedNut Mail

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



Albumin and glucose

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Albumin is a glycoprotein that is the primary, blood-specific carrier in the body's distribution network. It is not a glucose carrier. Increasing evidence indicates that interactions between albumin and glucose confer both benefit and harm.

Albumin-glucose interactions

1. Glycosylation

Glycosylation is the enzyme-driven binding of a sugar to specific amino acids. It is essential for albumin stability. That albumin could be glycosylated was only proven very recently. Consequently, the terms glycation and glycosylation continue to be applied interchangeably and the current glycosylation/glycation claims are unreliable.

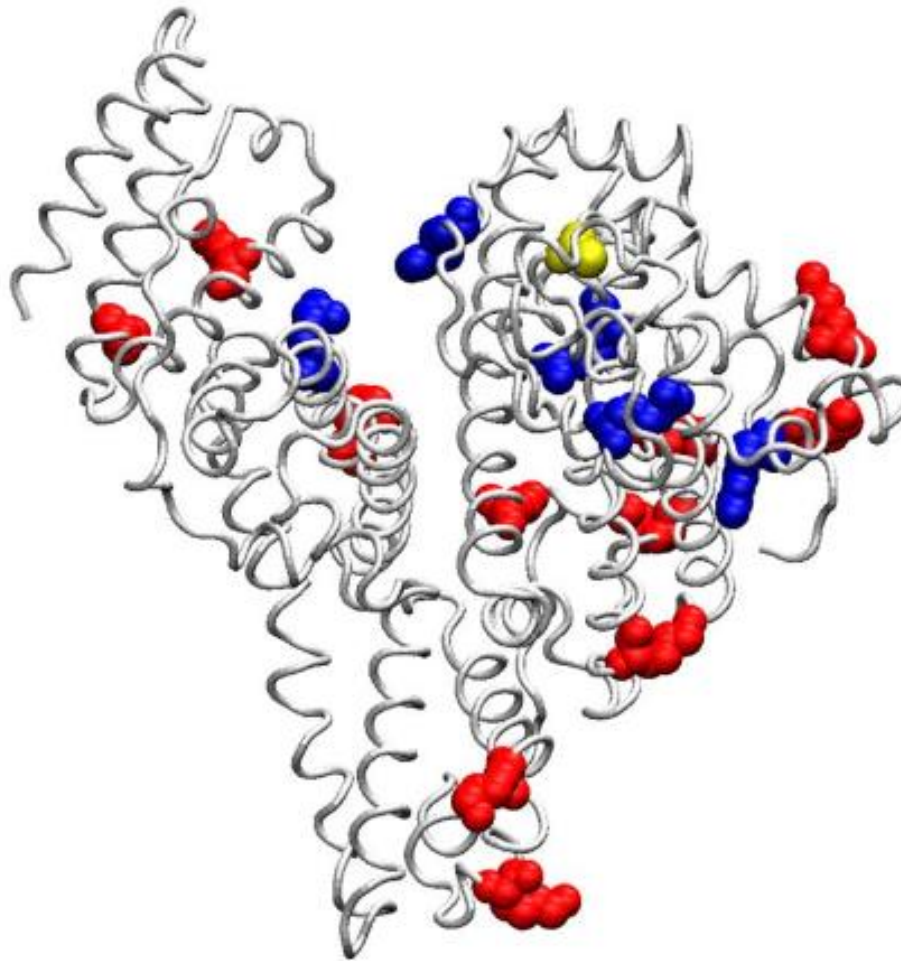
2. Glycation

Glycation is the non-enzymically driven binding of a sugar to a protein during hyperglycemia. Albumin contains more than 60 known glycation sites.

According to some reports, "normal" blood glycation levels are about 10-18%, and "diabetic" blood glycation levels are about 20-40%.

Identified glycation/glycosylation impacts include –

- decreased albumin binding of copper, zinc, iron and a range of other compounds including pharmaceuticals;
- inverse relationship between circulating vitamin D and glycated albumin levels;
- initiation of intracellular signaling;
- toxic impacts on microglia that may contribute to neurodegeneration;
- reduced binding affinity to bilirubin and long-chain fatty acids;
- reduced anti-oxidant properties via AGEs (advanced glycation end-products) formation, and consequent increased ROS (oxidative stress) formation;
- typically alters albumin's structure near Sudlow sites I+II;
- increased intrinsic structural flexibility of domains and secondary structure elements;
- increased albumin clearance.



The main sites of HSA modification. The sites of in vivo glycation are shown in red (lysines) and blue (arginines). The site of redox modification (Cys34) is shown in yellow.

From - **Serum Albumin in Health and Disease: Esterase, Antioxidant, Transporting and Signaling Properties**

<https://doi.org/10.3390/ijms221910318>

Glycation and nutrients

One of the factors that causes albumin glycation is impaired nutrient availability. Adequate availability of the following nutrients has been found to limit or inhibit albumin glycation – chromium, folate, magnesium, manganese, molybdenum, niacin, pyridoxine, retinol, thiamine, vitamin C, vitamin D metabolites (cholecalciferol and calcitriol), vitamin E, zinc. Their mechanisms of action are currently speculative.

Copper at physiological levels inhibits albumin glycation whilst both excessive and inadequate levels increase albumin glycation.

3. Glucuronidation

Glucuronidation is the covalent binding of acid glucuronide metabolites to albumin to create compounds that are highly hydrophilic. The binding can be reversible or irreversible and occurs in Sudlow's sites I+II.

Glucuronidation essentially supports the removal of unwanted substances from cells and the body by increasing their solubility.

The rate of glucuronidation is controlled by the rate by which glucuronides leave the cells. If glucuronidation rate is increased then so is their formation, and likewise reduced excretion rate means reduced formation. The rate of glucuronidation can directly and indirectly alter drug and nutrient availability and effectiveness.

Being highly hydrophilic, glucuronidation metabolites require transporters to move them through cell membranes. Key membrane transporters include [MRPs \(Multidrug resistant proteins\)](#), [BCRP \(breast cancer resistance protein\)](#), [OATPs \(organic anion transporting polypeptides\)](#), [OATs \(organic anion transporters\)](#), [OCTs \(organic cation transporters\)](#), BSEP (Bile salt export pump).

Factors that impair membrane transporters will consequently slow rate of glucuronidation.

Glucuronidation and nutrients

Some evidence indicates -

- iron and arachidonic acid can indirectly alter glucuronidation via the glucuronosyltransferases (UGTs);
- high-dose vitamin A inhibits UGTs and therefore glucuronidation;
- vitamin D modulates extrahepatic glucuronosyltransferase activity.

Clinical Concerns

Speculatively, glycated albumin is a potential mal-nutrition marker. If glycated albumin levels are raised, then we should ascertain whether there is a nutritional contribution. If the Diet History indicates adequate dietary intake of all key nutrients, then direct nutritional contribution is unlikely. However, non-nutritional factors may alter nutrient availability indirectly via mechanisms of action such as inhibition of the membrane transporters.

Albumin and glucose

Many commonly prescribed drugs have been found to impair availability of one or more nutrients associated with inhibiting glycation. For example, clozapine, doxepin, imipramine, and olanzapine inhibit chromium availability.

Polypharmacy combinations often negatively impact one or more common nutrients. Examples include –

- both Proton Pump Inhibitor + metformin negatively impact availability of magnesium, thiamine, and vitamin C;
- Proton Pump Inhibitor + furosemide + digoxin all negatively impact magnesium availability.

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 -

- consider requesting glycated albumin as a mal-nutrition marker? And how would you interpret, and act on, the results?
- clarify adequacy of total intake of all nutrients, including both dietary choices and nutrient supplements if glycated albumin is elevated?
- clarify and regularly monitor copper, iron, zinc, and vitamin D levels if glycated albumin is elevated?

Conclusions

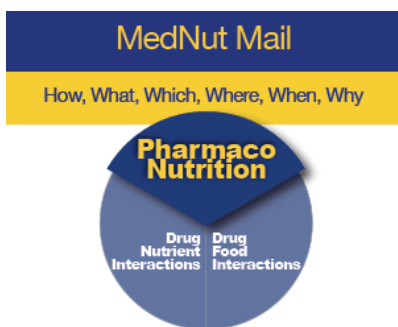
Albumin and glucose interact via glycosylation, glycation and glucuronidation. These interactions typically alter albumin's structure and consequently alter nutrient and drug availability.

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.

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