



**Letter: albumin - does formulation matter? Authors' reply**

Journal:	<i>Alimentary Pharmacology &amp; Therapeutics</i>
Manuscript ID	Draft
Wiley - Manuscript type:	Letter to the Editors
Date Submitted by the Author:	n/a
Complete List of Authors:	Gutiérrez-Valencia, Marta; Navarre Health Service, Unit of Innovation and Organization Leache, Leire; Navarre Health Service, Unit of Innovation and Organization Saiz, Luis Carlos; Navarre Health Service, Unit of Innovation and Organization Uriz, Juan; Hospital Universitario de Navarra, Department of Gastroenterology and Hepatology Bolado, Federico; University Hospital of Navarre, Department of Gastroenterology and Hepatology García-Erce, José Antonio; Navarre Health Service, Navarra's Blood and Tissue Bank Cantarelli, Lorenzo; University Hospital of Canary Islands (CHUC), Department of Hospital Pharmacy Erviti, Juan; Navarre Health Service, Unit of Innovation and Organization
Keywords:	Cirrhosis < Hepatology, Clinical pharmacology < Topics, Ascites < Hepatology, Liver < Organ-based

SCHOLARONE™  
Manuscripts

This is the peer reviewed version of the following article: Leache, L., Gutiérrez-Valencia, M., Saiz, L.C., Uriz, J., Bolado, F., García-Erce, J.A., Cantarelli, L. and Erviti, J. (2023), Letter: Albumin—Does formulation matter? Authors' reply. *Aliment Pharmacol Ther*, 57: 1484-1485. <https://doi.org/10.1111/apt.17546> which has been published in final form at <https://doi.org/10.1111/apt.17546>. This article may be used for non-commercial purposes in accordance with Wiley Terms and Conditions for Use of Self-Archived Versions. This article may not be enhanced, enriched or otherwise transformed into a derivative work, without express permission from Wiley or by statutory rights under applicable legislation. Copyright notices must not be removed, obscured or modified. The article must be linked to Wiley's version of record on Wiley Online Library and any embedding, framing or otherwise making available the article or pages thereof by third parties from platforms, services and websites other than Wiley Online Library must be prohibited.

**Letter: albumin - does formulation matter? Authors' reply**

Dear editor,

We thank Dr. Yu and colleagues for their interest in our publication.<sup>1</sup>

It is well known that retention of sodium and water is a key factor in the pathogenesis of ascites.<sup>2</sup> Based on this, we believe that the reflection seems interesting and the hypothesis about the influence of the sodium content of albumin preparations on the results is theoretically feasible. However, we think that the impact would not be too relevant when compared to other mentioned contributing factors such as different study populations, diuretic management or albumin treatment patterns.

Current guidelines recommend a moderate restriction of sodium intake (80–120 mmol/day) in cirrhotic patients with ascites, and state that diets with a very low sodium content should be avoided, as they are associated with more complications and can endanger patient's nutritional status.<sup>2,3</sup> Albumin doses proposed in the randomized controlled trials on long-term albumin do not exceed 40 g weekly or every two weeks. Assuming a mean sodium concentration of 120-130 mmol/L with 20% albumin, this would mean a maximum of 24-26 mmol weekly, which does not seem to be so excessive considering a limit of 120 mmol/day. The authors have selected a limited number of formulations among those available (specific criteria for this choice are not provided), which also have a wide range of sodium concentration, and probably contain an intermediate amount.

Furthermore, to our knowledge, this sodium content hypothesis has not been supported by any comparative study with any type of design, nor is it evident to draw this conclusion from the available clinical trials based on the albumin they use.

The studies by Gentilini et al.<sup>4</sup> and Romanelli et al.<sup>5</sup> do not provide any information about the albumin supplier or formulation. Wilkinson & Sherlock<sup>6</sup> mention that they used salt-poor human serum-albumin (Lister Institute) (sodium content unknown, study published in 1962). On the other hand, the study by Caraceni et al.,<sup>7</sup> which reports the best results with long-term albumin, was supplied by different companies according to the Italian legislation on non-profit trials, so they used a variety of formulations with different sodium contents. This study obtained promising findings without apparently using the aforementioned formulation of albumin with very low sodium concentration.

Therefore, in our opinion, there may be other factors that may account to a greater extent for the differences in trials' results. These would include the degree of severity/ascitic decompensation status of patients, amount and frequency of albumin administered in each study, requirements and management of diuretics, and dietary sodium intake in each study.

It seems a cautious approach that albumin should not have an excessive sodium content. To shed new light on this issue, it would be desirable to explore Yu and colleagues' hypothesis by conducting a comparative study contrasting different presentations of albumin.

1. Leache L, Gutiérrez-Valencia M, Saiz LC, et al. Meta-analysis: Efficacy and safety of albumin in the prevention and treatment of complications in patients with cirrhosis. *Aliment Pharmacol Ther.* 2023;57(6):620-634. doi:10.1111/APT.17344
2. Aithal GP, Palaniyappan N, China L, et al. Guidelines on the management of ascites in cirrhosis. *Gut.* 2021;70(1):9-29. doi:10.1136/GUTJNL-2020-321790
3. Angeli P, Bernardi M, Villanueva C, et al. EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. *J Hepatol.* 2018;69(2):406-460. doi:10.1016/j.jhep.2018.03.024
4. Gentilini P, Casini-Raggi V, Fiore G Di, et al. Albumin improves the response to diuretics in patients with cirrhosis and ascites: Results of a randomized, controlled trial. *J Hepatol.* 1999;30(4):639-645. doi:10.1016/S0168-8278(99)80194-9
5. Romanelli RG, La Villa G, Barletta G, et al. Long-term albumin infusion improves survival in patients with cirrhosis and ascites: an unblinded randomized trial. *World J Gastroenterol.* 2006;12(9):1403-1407. <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med6&NEWS=N&AN=16552809>
6. Wilkinson P, Sherlock S. The effect of repeated albumin infusions in patients with cirrhosis. *Lancet.* 1962;280(7266):1125-1129. doi:10.1016/S0140-6736(62)90895-4
7. Caraceni P, Riggio O, Angeli P, et al. Long-term albumin administration in decompensated cirrhosis (ANSWER): an open-label randomised trial. *Lancet.* 2018;391(10138):2417-2429. doi:10.1016/S0140-6736(18)30840-7