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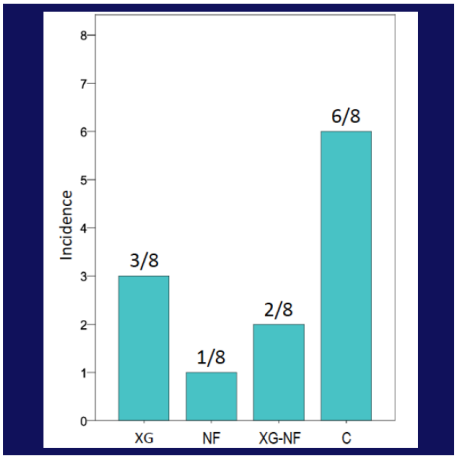
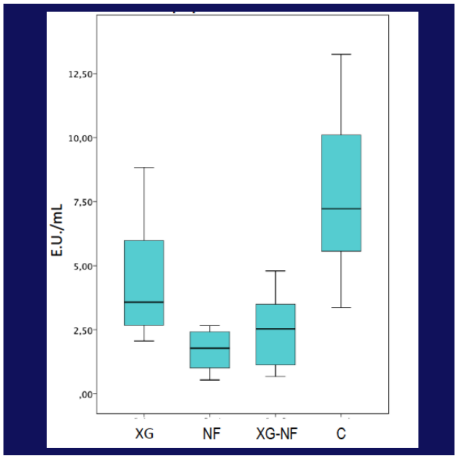
Xyloglucan Protects the Intestinal Barrier and Reduces Bacterial Translocation in Experimental Cirrhosis: A Promising Non-Antibiotic Strategy

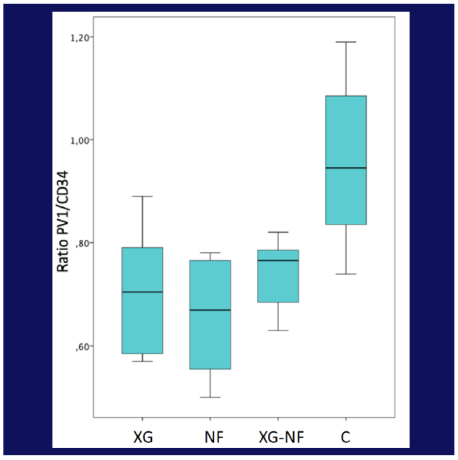
Bacterial translocation



Endotoxemia



Vascular integrity



XG, xyloglucan; NF, norfloxacin; XG-NF, xyloglucan and norfloxacin; C, control

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Xyloglucan protects the intestinal barrier and reduces bacterial translocation in experimental cirrhosis - A promising non-antibiotic strategy

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Keywords: Xyloglucan. Norfloxacin. Bacterial translocation. Gut-liver axis. Animal model.

Abbreviations:

- **ACLF:** Acute-on-chronic liver failure
- **BT:** Bacterial translocation
- **CMCiB:** Comparative Medicine and Bioimage Centre of Catalonia
- **IFN-γ:** Interferon gamma
- **IL:** Interleukin
- **LPS:** Lipopolysaccharide

- **MDR:** Multidrug-resistant
- **NF:** Norfloxacin
- **PV1:** plasmalemma vesicle-associated protein 1
- **SBP:** Spontaneous bacterial peritonitis
- **TNF-α:** Tumor necrosis factor alfa
- **XG:** Xyloglucan

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Authors contribution: Conceptualization, I.I., R.B., H.M. and R.M.; methodology, I.I., R.B., H.M. and R.M.; validation, R.B.; formal analysis, I.I. and R.B.; investigation, I.I. and R.B.; resources, R.B.; data curation, I.I. and R.B.; writing—original draft preparation, I.I., R.B., H.M. and R.M.; writing—review and editing, all authors contributed. All authors have read and agreed to the published version of the manuscript

Data availability: The data underlying this article will be shared on reasonable request to the corresponding authors.

Ethics approval: All animal experiments adhered to European regulations and received the approval of the CMCiB Animal Experimentation Ethical Committee and local authorities (Generalitat de Catalunya, project authorization nº 10490).

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Abstract:

Background: Cirrhosis alters the intestinal barrier, increasing permeability and promoting bacterial translocation (BT). Norfloxacin is currently the only effective strategy to reduce BT, but the rise of multidrug-resistant bacteria highlights the need for new approaches.

Aims: To evaluate the effect of xyloglucan, alone or with norfloxacin, on the intestinal barrier in cirrhotic rats with ascites.

Methods: Decompensated cirrhosis with ascites was induced in 32 rats using CCl4. They were then administered xyloglucan (XG), norfloxacin (NF), xyloglucan+norfloxacin (XG+NF), or water (control) for one week. Parameters measured included BT incidence, endotoxemia, IFN-γ, IL-23, PV1/CD34 ratio, occludin and liver histology.

Results: BT incidence was lower in all treatment groups (XG, NF, XG+NF) compared to controls, and significantly so in NF and XG+NF. Endotoxemia was reduced significantly in all treatment groups compared to controls, with values correlating significantly with BT incidence, occludin expression, IFN-γ levels, IL-23 levels, and PV1/CD34 ratio. There were no differences in IL-23 levels, but all treatment groups exhibited a decrease in IFN-γ, which was significant in the NF and XG+NF groups. All treatment groups showed significant increases in occludin levels and decreases in PV1/CD34 ratio compared to controls. All groups showed similar histological signs of cirrhosis.

Conclusions: Xyloglucan reduces intestinal mucosal inflammation, improves mucosal integrity and vascular permeability, and reduces endotoxemia and BT incidence. Xyloglucan alone showed similar results to norfloxacin; however, combining xyloglucan with norfloxacin does not provide additional benefits. These findings support evaluating xyloglucan as a new therapeutic strategy to prevent infections in cirrhosis.

Abstract word count: 246 words

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Lay summary:

Cirrhosis is a chronic liver disease that can weaken the intestinal barrier, allowing bacteria from the gut to enter the bloodstream, a process known as bacterial translocation. This contributes to severe infections and worsens the condition of people living with cirrhosis. Currently, the antibiotic norfloxacin is one of the few treatments available to prevent this process. However, the increasing problem of antibiotic resistance makes it important to explore alternative, non-antibiotic strategies.

In this study we tested the effects of xyloglucan, a plant-based compound known for forming a protective film over the intestinal lining. The experiment was conducted in rats with advanced cirrhosis. The animals were treated with xyloglucan alone, norfloxacin alone, both combined, or no treatment.

The results showed that xyloglucan helped strengthen the gut barrier, reduced signs of inflammation, and lowered the amount of bacteria entering the bloodstream. These effects were similar to those achieved with norfloxacin. Unfortunately, combining both treatments did not lead to greater benefits than using either one alone.

These findings suggest that xyloglucan could be a promising new tool for preventing infections in cirrhosis, offering a potential alternative or complement to antibiotics, especially in a context where antibiotic resistance is becoming an urgent concern.

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1. Background:

1.1 Bacterial infections in cirrhosis:

Bacterial infections are a common complication in cirrhotic patients, occurring in up to one-third of patients upon hospital admission or during hospitalization[1]. These events directly increase the risk of cirrhosis decompensation, developing acute-on-chronic liver failure (ACLF) and mortality [1,2].

1.2 Bacterial translocation:

The key pathogenic mechanism underlying infections in cirrhosis is bacterial translocation (BT), which is defined as the passage of viable bacteria or their products from the gastrointestinal tract to the mesenteric lymph nodes[3,4].

The scarring of the hepatic parenchyma in cirrhosis derives into a decrease in biliary acid synthesis and other metabolic disorders that result in bacterial overgrowth and a characteristic dysbiosis[5,6]. The increased presence of certain Gram-negative bacteria (GNB) results in the translocation of endotoxins that stimulate the gut-associated lymphoid tissue[7] to secrete proinflammatory cytokines such as TNF-α, IL-1β, IL-23 and IFN-γ[8] and decreases the production of anti-inflammatory cytokines such as IL-22[9]. Additionally, endotoxins and proinflammatory cytokines upregulate the presence of plasmalemma vesicle-associated protein 1 (PV-1) an endothelial membrane protein responsible for pore formation in the vascular epithelium[10]. An elevated PV1/CD34 ratio correlates directly with vascular damage and leakage[10].

The presence of endotoxins and proinflammatory cytokines leads to a disruption of tight-junctions, which is intrinsically related to a pathological increase in intestinal permeability and BT[11].

1.3 Therapeutic strategies

Prophylaxis against BT is crucial for preventing bacterial infections, particularly spontaneous bacterial peritonitis. At present, the only recommended prophylactic treatment is selective intestinal decontamination using norfloxacin (NF)[12], which

reduces the risk of new spontaneous bacterial peritonitis (SBP) episodes from 70% to 20% by decreasing GNB in intestinal microbiota[13].

However, long-term use of NF in these patients entails a heightened risk of infections by gram-positive cocci, particularly SBP. This fact, along with the increase in invasive procedures, extensive use of third-generation cephalosporins, and greater exposure to the hospital environment, has led to a rise in infections caused not only by gram-positive cocci but also by fungi and, notably, multidrug-resistant (MDR) bacteria[14,15], which has strong implications in the prognosis of these patients.

1.4 Potential of xyloglucan

Xyloglucan (XG) is a water-soluble non-digestible hemicellulose of plant origin, which is part of a new class of compounds termed "mucosal protectors". XG is proposed to act as a barrier due to its mucoadhesive properties, forming a protective film in the intestinal mucus layer and shielding the mucosa from chemical or bacterial aggression. This mechanism prevents bacterial adherence to the epithelium and maintains normal permeability and secretion.

Previous in vitro studies have revealed its capacity to preserve tight-junctions and paracellular flow by forming a mucin-like layer, thereby shielding the epithelium from chemical or bacterial aggression, and preventing bacterial adhesion[16,17]. Commercialized medical devices based on XG compounds have demonstrated success in treating acute[18,19] and chronic diarrhea[20,21] and preventing urinary tract infections[22,23].

1.5 Hypothesis and aims:

We hypothesized that XG's protective effects might counteract the disruptions to the epithelial and vascular barriers seen in cirrhosis, ultimately decreasing BT. The aims of this study were, first, to evaluate the effect of XG (alone or in combination with NF) on BT in a rat model of CCl_4-induced cirrhosis with asicites; and second, to assess its structural effect on the epithelial and vascular barrier.

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2. Materials and methods:

2.1 Cirrhosis induction:

Cirrhosis was induced to Sprague-Dawley rats using the Runyon model of CCl_4 orogastric administration[24]. Animals had *ad libitum* access standand chow and autoclaved drinking water, supplemented with phenobarbital (5 mmol/L) as a hepatic metabolic inducer.

Following a two-week acclimation period, CCl_4 was administered weekly though a stainless steel orogastric cannula (Popper & Sons, NY, USA) with 0.5 mL of water. Briefly, CCl_4 administered doses were adjusted based on the weight difference 48 hours post-administration and just before the next administration. The damage induced in the liver parenchyma led to a decrease in metabolism and resulted in a reduction of the toxic effects of CCl_4[25], therefore an extra dose increase was set after several weeks.

When ascites was suspected by abdominal distension, an abdominal paracentesis using a 25G needle under inhaled isoflurane anesthesia was carried out to confirm the diagnosis. The presence of ascites was considered a confirmatory sign of cirrhosis with portal hypertension.

2.2 Experimental treatment

Upon confirmation of cirrhosis, animals were allocated sequentially to assemble 4 groups of 8 animals: Group XG) Gelsectan 70mg/kg (equivalent to xyloglucan 12.5 mg/kg), Group NF) Norfloxacin 5 mg; Group XG+NF) Gelsectan 70mg/kg and norfloxacin 5 mg; Control group) Water 1 mL. Blinding was not implemented, as it was deemed unnecessary.

Gelsectan (Noventure, Barcelona, Spain) is a commercialized product approved for the treatment and prevention of acute and chronic diarrhea, abdominal pain, bloating and flatulence. Every capsule contains 100 mg of XG, 250 mg of pea protein cross-linked with grape seed extract, and 210 mg of xylooligosaccharide.

In the treatment groups (XG, NF and XG+NF), each animal received the assigned treatment diluted in 1mL of water using a stainless steel orogastric cannula (Popper & Sons, NY, USA) daily for a week. The control group was administered 1mL of water following the same procedure.

After one week of treatment, animals were euthanized by anesthetic overdose. Endotoxin levels were evaluated from portal blood samples. To evaluate BT, mesenteric lymph nodes were collected, processed and cultured. Cecum samples were obtained to assess inflammatory activity (IFN-γ and IL-23), vascular integrity (PV1/CD34 ratio) and epithelial integrity (ocludine relative expression). Finally, liver samples were collected and stained with haematoxylin & eosin and Masson's trichrome for the histological evaluation of cirrhosis following the Batts and Ludwig scoring system[26].

2.3 Statistical analysis

Quantitative data are presented as mean +/- standard deviation unless otherwise indicated; categorical data are presented as proportions. The Shapiro-Wilk test was used to assess normal distribution, and Levene's test was used to assess variance equality. Quantitative data were compared using either Student's T-test and the ANOVA test or the Mann-Whitney U-test and the Kruskall Wallis test, depending on variance equality. The Bonferroni correction and the Dunn test were applied for multiple comparisons where applicable. Proportions were compared using the χ^2 test or Fisher's exact test depending on normal distribution. The correlation between quantitative variables was evaluated using Spearman's rank correlation coefficient or Pearson correlation coefficient (r), with results stratified into moderate (r=0.3-0.5), strong (r=0.5-0.7), and very strong correlations (r>0.7)[27]. A p value lower than 0.05 was considered statistically significant. The statistical analysis was performed using SPSS (version 23.0) for Windows software (Chicago, IL, USA).

3. Results

3.1 Bacterial translocation

BT was observed in 12 out of 32 rats (37.5%). In the control group, BT was detected in 6 out of 8 rats (75%), accounting for half of the total BT episodes. The remaining 6 episodes were distributed among the treatment groups: 3 in the XG group (37.5%), 1 in the NF group (12.5%) and 2 in the XG + NF group (25%). While BT incidence was lower in all treatment groups compared to controls, statistically significant differences were only noted in the NF and XG+NF groups (XG p=0.130; NF p=0.012; XG+NF p=0.045) (Fig. 1.A).

Furthermore, animals that developed BT exhibited significantly higher levels of endotoxemia (6.49±3.77 vs. 2.66±1.47 UE/mL; p=0.004) and IL-23 (21.58±10.16 vs. 14.62±6.61 pg/mL; p=0.036), lower levels of occludin (0.47±0.10 vs. 0.57±0.08; p=0.016), and a higher PV1/CD34 ratio (0.85±0.20 vs. 0.71±0.11; p=0.015); no differences were observed in the levels of IFN-γ (94.44±32.66 vs. 77.25±23.58 pg/mL; p=0.095) nor in the histological scores (10.42±1.00 vs. 10.75±1.02; p=0. 374).

3.2 Endotoxin levels

Endotoxin levels (UE/mL) were significantly reduced in all treatment groups compared to controls (XG 4.42±2.32, p=0.021; NF 1.70±0.83, p=0.001; XG+NF 2.47±1.47, p=0.002; Control 7.80±3.22). Animals receiving NF showed the lowest levels of endotoxin and significant differences were found not only with the control group but also with those that received XG (Fig. 1.B).

Correlation tests involving endotoxin levels revealed a very strong correlation with IFN-γ levels (r=0.746, p<0.01); a strong correlation with BT incidence (r=0.510, p<0.01) and PV1/CD34 ratio (r=0.583, p<0.01); and a moderate correlation with occludin expression (r=0.434, p<0.05) and IL-23 levels (r=0.440, p<0.05) (Fig. 2).

3.3 Proinflammatory cytokines

All four groups exhibited similar IL-23 values (pg/mL) (XG 17.78±9.25, NF 14.88±5.26, XG+NF 15.87±7.89, Control 20.39±11.72; p =0.62), with no significant differences observed either between treatments or compared to controls (Fig. 1.E). Higher levels of IL-23 were detected in rats with BT (21.58±10.16 vs. 14.62±6.61 pg/mL; p=0.036).

IFN-γ levels (pg/mL) in the treatment groups were lower than in controls (XG 87.96±25.57, p=0.590; NF 65.02±15.25, p=0.007; XG+NF 73.47±32.61, p=0,041; Control 108.33±17.89), with statistically significant differences observed only in the NF and XG+NF groups (Fig.1.D).

3.4 Vascular barrier integrity

PV1/CD34 ratio was significantly decreased in the three treatment groups compared to controls (XG 0.71±0.12, p=0.002; NF 0.69±0.09, p=0.001; XG+NF 0.70±0.10, p=0.002; Control 0.96±0.16). Similar to previous determinations, no significant differences were noted between the treatment groups (Fig. 1.F).

3.5 Epithelial integrity

All treatment groups showed a significant increase in the relative expression of occludin compared to controls in the cecum mucosa, with no differences observed between them (XG 0.59±0.06, p<0.001; NF 0.49±0.03, p=0.037; XG+NF 0.63±0.06, p<0.001; Control 0.41±0.03) (Fig. 1.C).

3.6 Liver histology

Characteristic signs of well-established cirrhosis were observed in all animals. No differences were evident according to the Batts and Ludwig score system between the four groups: XG 10.75±0.89, NF 10.88±0.99, XG+NF 10.75±1.04, Control 10.13±1.13 (p =0.457) (Fig. 3).

4. Discussion

Bacterial infections represent a serious threat to the prognosis of patients with cirrhosis associated with high morbidity, mortality and ACLF[28,29]. As mentioned before, BT is the main mechanism of infections in these patients, and currently selective intestinal decontamination with NF stands as the sole recommended treatment in the prophylaxis of SBP[12,30,31]. However, this approach entails changes in epidemiological

patterns, reduced efficacy of conventional antibiotic therapies and increased risk for development of infections caused by MDR bacteria[14,15]. This highlights the necessity of reevaluating treatment and prophylaxis strategies aside from antibiotics in patients with cirrhosis.

The introduction of "mucosal protective" compounds such as XG holds promise as a solution to this problem, given its mucine-like features. In this experiment, we assessed the impact of XG both alone and in combination with NF on the prevention of BT and the underlying mechanisms leading to it. As expected, the development of BT was accompanied by a significant elevation of endotoxemia, as well as an increase in IL-23 and a significant disruption of the integrity of both the epithelial and vascular barriers. All treatment groups (groups XG, NF and XG+NF) exhibited a decrease in BT compared to controls, with statistically significant reductions observed only in the groups receiving NF (groups NF and NF+XG).

The administration of XG alone (group XG) significantly reduced endotoxemia in portal blood compared to controls; however, treatment with NF alone (group NF) reduced said levels significantly more than XG alone. Moreover, the addition of XG to NF failed to show any significant improvement in the reduction of endotoxemia or in BT incidence compared to NF alone.

All treatment groups showed lower levels of colonic IFN-γ, again with significant differences observed only in the NF-receiving groups (groups NF and XG+NF). It was previously described that the presence of high levels of IFN-γ might lead to decreased stability of the intestinal epithelia favoring bacterial translocation[32].

However, no differences in IL-23 levels were found in any group. In this sense, it has been reported that serum levels of IL-23 correlate significantly with the degree of liver damage, being significantly elevated in patients with well-established cirrhosis[33]. All animals had well-established cirrhosis (F4) with a similar Batts and Ludwig score, which may explain these results.

Regarding intestinal barrier integrity, all treatment groups (groups XG, NF and XG+NF) showed significant improvements in the relative expression of occludin (mucosal

integrity) and the PV1/CD34 ratio (vascular integrity) compared to controls. As previously described in murine models of cirrhosis (CCl_4 and bile duct ligation models), the administration of NF was associated with and increased expression of some tight-junction proteins (TJP-1 and occludin)[35].

Our findings suggest that XG exerts a protective effect on the intestinal barrier, reduces the inflammation of the intestinal mucosa, and improves both mucosal integrity and vascular permeability. However, compared to the standard approach with NF, XG alone achieved similar improvements in mucosal integrity and vascular permeability (as indicated by occludin and PV1/CD34 ratio) but proved less effective in reducing bacterial translocation and inflammation (as measured by endotoxemia and IFN-γ levels). Moreover, the addition of XG to NF treatment did not show any supplementary advantage over the administration of NF alone.

It is important to acknowledge certain limitations of our study. First, this is a proof-of-concept experiment, conducted with small groups of animals and assessing only one XG dosage due to limited evidence. Additionally, XG was not administered alone and results may be affected by the other components of gelsectan. Last, despite the pathophysiological similarities between the animal model and cirrhosis in humans, the inherent limitations of animal experimentation may affect its translatability to patients with cirrhosis.

In conclusion, the emergence of infections caused by multidrug-resistant bacteria presents a significant challenge in the prophylaxis and treatment of infections in cirrhosis. Therefore, the development of new strategies beyond antibiotics is imperative. XG is a promising alternative for preventing BT and subsequently infections in cirrhotic patients. Further research is required to evaluate how the protective effects of XG on the intestinal barrier may influence the development of cirrhosis decompensation, ACLF and mortality.

5. References

1. Borzio M, Salerno F, Piantoni L, et al. Bacterial infection in patients with advanced cirrhosis: a multicentre prospective study. Dig Liver Dis [Internet] 2001;33(1):41–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11303974

2. Arvaniti V, D'Amico G, Fede G, et al. Infections in patients with cirrhosis increase mortality four-fold and should be used in determining prognosis. Gastroenterology 2010;139(4):1246–56, 1256.e1-5.
3. Muñoz L, Borrero M, Úbeda M, et al. Intestinal Immune Dysregulation Driven by Dysbiosis Promotes Barrier Disruption and Bacterial Translocation in Rats With Cirrhosis. Hepatology 2019;70(3):925–38.
4. Van der Merwe S, Chokshi S, Bernsmeier C, Albillos A. The multifactorial mechanisms of bacterial infection in decompensated cirrhosis. J Hepatol 2021;75:S82–100.
5. Chang C-S, Chen G-H, Lien H-C, Yeh H-Z. Small intestine dysmotility and bacterial overgrowth in cirrhotic patients with spontaneous bacterial peritonitis. Hepatology 1998;28(5):1187–90.
6. Bauer TM, Schwacha H, Steinbruckner B, et al. Small intestinal bacterial overgrowth in human cirrhosis is associated with systemic endotoxemia. Am J Gastroenterol 2002;97(9):2364–70.
7. Lang S, Schnabl B. Microbiota and Fatty Liver Disease—the Known, the Unknown, and the Future. Cell Host Microbe 2020;28(2):233–44.
8. Al-Sadi R, Ye D, Dokladny K, Ma TY. Mechanism of IL-1beta-induced increase in intestinal epithelial tight junction permeability. J Immunol 2008;180(8):5653–61.
9. Chiang H-Y, Lu H-H, Sudhakar JN, et al. IL-22 initiates an IL-18-dependent epithelial response circuit to enforce intestinal host defence. Nat Commun 2022;13(1):874.
10. Shue EH, Carson-Walter EB, Liu Y, et al. Plasmalemmal Vesicle Associated Protein-1 (PV-1) is a marker of blood-brain barrier disruption in rodent models. BMC Neurosci 2008;9(1):29.
11. Luissint A-C, Parkos CA, Nusrat A. Inflammation and the Intestinal Barrier: Leukocyte–Epithelial Cell Interactions, Cell Junction Remodeling, and Mucosal Repair. Gastroenterology 2016;151(4):616–32.
12. 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):406–60.
13. Mücke MM, Mücke VT, Graf C, et al. Efficacy of Norfloxacin Prophylaxis to Prevent Spontaneous Bacterial Peritonitis: A Systematic Review and Meta-Analysis. Clin Transl Gastroenterol 2020;11(8):e00223.
14. Fernández J, Acevedo J, Castro M, et al. Prevalence and risk factors of infections by multiresistant bacteria in cirrhosis: A prospective study. Hepatology 2012;55(5):1551–61.
15. De Mattos AA, Costabeber AM, Lionço LC, Tovo CV. Multi-resistant bacteria in spontaneous bacterial peritonitis: A new step in management? World J Gastroenterol. 2014;20(39):14079–86.
16. De Servi B, Ranzini F, Piqué N. Effect of Utipro® (containing gelatinxyloglucan) against Escherichia coli invasion of intestinal epithelial cells: Results of an in vitro study. Future Microbiol 2016;11(5):651–8.
17. Piqué N, Gómez-Guillén M del C, Montero MP. Xyloglucan, a plant polymer with barrier protective properties over the mucous membranes: An overview. Int J Mol Sci. 2018;19(3).
18. Gnessi L, Bacarea V, Marusteri M, Piqué N. Xyloglucan for the treatment of acute diarrhea: Results of a randomized, controlled, open-label, parallel group, multicentre, national clinical trial. BMC Gastroenterol 2015;15(1).
19. Pleșea Condratovici C, Bacarea V, Piqué N. Xyloglucan for the Treatment of Acute Gastroenteritis in Children: Results of a Randomized, Controlled, Clinical Trial. Gastroenterol Res Pract 2016;2016:1–7.
20. Alexea O, Bacarea V, Piqué N. The combination of oligo- and polysaccharides and reticulated protein for the control of symptoms in patients with irritable bowel syndrome: Results of a randomised, placebo-controlled, double-blind, parallel group,

multicentre clinical trial. United European Gastroenterol J 2016;4(3):455–65.
21. Trifan A, Burta O, Tiuca N, Petrisor DC, Lenghel A, Santos J. Efficacy and safety of Gelsectan for diarrhoea-predominant irritable bowel syndrome: A randomised, crossover clinical trial. United European Gastroenterol J 2019;7(8):1093–101.
22. Esposito E, Campolo M, Casili G, et al. Efficacy of Xyloglucan against <i>Escherichia coli</i> Extraintestinal Urinary Tract Infection: An in vivo Study. Microb Physiol 2020;30(1–6):50–60.
23. Kostev K, Cai T. Cystitis and Utipro® Plus: Real-World Evidence. Healthcare 2023;11(18):2564.
24. Runyon BA, Sugano S, Kanel G, Mellencamp MA. A rodent model of cirrhosis, ascites, and bacterial peritonitis. Gastroenterology 1991;100(2):489–93.
25. Das PK, Chopra P, Nayak NC. Hepatocellular tolerance to carbon tetrachloride induced injury in the rat: A study of its nature and possible mode of evolution. Exp Mol Pathol 1974;21(2):218–36.
26. Batts KP, Ludwig J. An Update on Terminology and Reporting. Am J Surg Pathol 1995;19(12):1409–17.
27. Kuckartz U, Rädiker S, Ebert T, Schehl J. Statistik: Eine verständliche Einführung. Springer; 2013. p. 213.
28. D'Amico G, Morabito A, D'Amico M, et al. Clinical states of cirrhosis and competing risks. J Hepatol. 2018;68(3):563–76.
29. Piano S, Bunchorntavakul C, Marciano S, Rajender Reddy K. Infections in cirrhosis. Lancet Gastroenterol Hepatol 2024;
30. Runyon BA. Management of adult patients with ascites due to cirrhosis. Hepatology 2004;39(3):841–56.
31. Rimola A, García-Tsao G, Navasa M, et al. Diagnosis, treatment and prophylaxis of spontaneous bacterial peritonitis: a consensus document. J Hepatol 2000;32(1):142–53.
32. Vega-Magaña N, Delgado-Rizo V, García-Benavides L, et al. Bacterial Translocation Is Linked to Increased Intestinal IFN-γ, IL-4, IL-17, and mucin-2 in Cholestatic Rats. Ann Hepatol 2018;17(2):318–29.
33. Yang X, Liao L, Liang Z, Yu S, Guo Z. Correlation Analysis of IL-17, IL-21, IL-23 with Non-Alcoholic Liver Fibrosis and Cirrhosis. J Inflamm Res 2024;Volume 17:2327–35.
34. Riva A, Gray EH, Azarian S, et al. Faecal cytokine profiling as a marker of intestinal inflammation in acutely decompensated cirrhosis. JHEP Reports 2020;2(6):100151.
35. Gómez-Hurtado I, Moratalla A, Moya-Pérez Á, et al. Role of interleukin 10 in norfloxacin prevention of luminal free endotoxin translocation in mice with cirrhosis. J Hepatol 2014;61(4):799–808.

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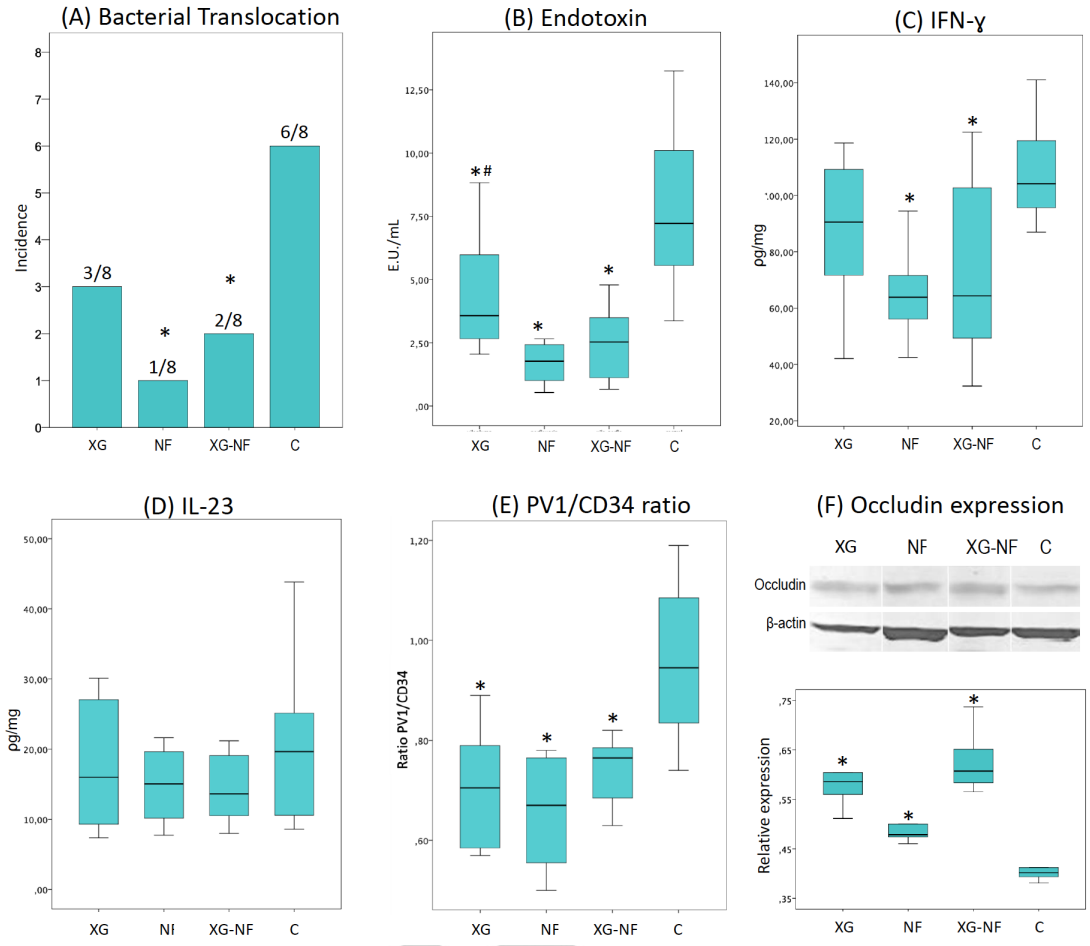

Fig. 1 Results: (A) Bacterial translocation incidence. (B) Endotoxin levels (EU/mL) in portal blood. (C) IFN-γ levels (pg/mL) in colonic tissue (ELISA). (D) IL-23 levels (pg/mL) in colonic tissue (ELISA). (E) PV1/CD34 ratio in colonic tissue (ELISA). (F) Top: Western Blot example in one rat of each group of occludin and β-actin (loading control); bottom: relative expression of occludin in colonic tissue. Bars represent standard deviation and bold lines inside the box plot median values. *p<0.05 compared to controls #p<0.05 compared to norfloxacin alone; XG, xyloglucan group; NF, norfloxacin group; XG-NF, xyloglucan and norfloxacin group; C, control group.

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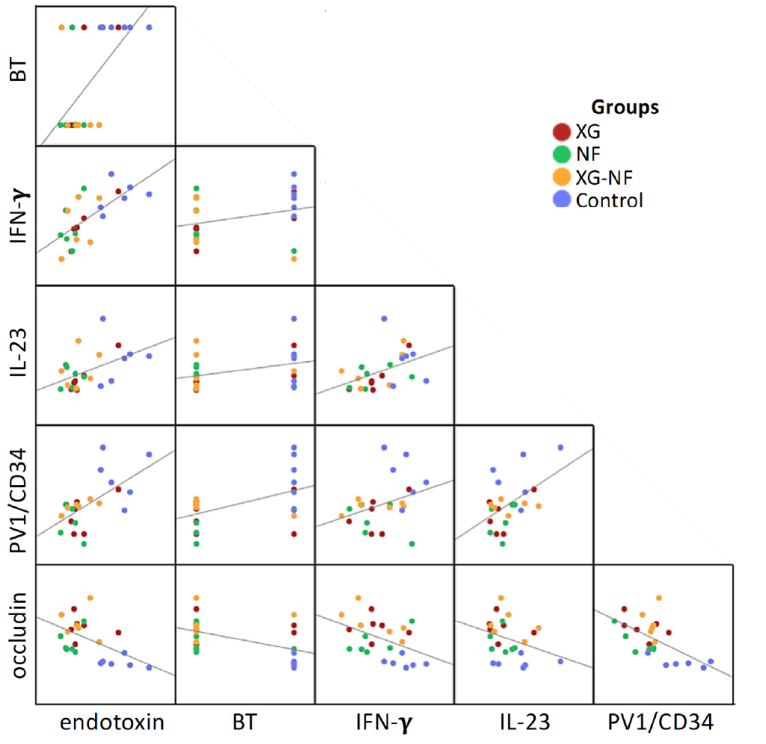

Correlation r value (95%IC)	Endotoxin	BT	IFN-δ	IL-23	PV1/CD34 ratio
BT	0,510** (,197-,729)				
IFN-δ	0,746** (,537-,868)	0,308 (-,0,045-0,593)			
IL-23	0,440* (,108-,683)	0,378* (0,034-0,642)	0,419* (0,083-0,669)		
PV1/CD34 ratio	0,583** (,295-,774)	0,318* (-0,034-0,6)	0,378* (0,034-0,642)	0,379* (0,035-0,642)	
Occludin	-0,434* (-0,0712- -0,038)	-0,485* (-0,743- -0,102)	-0,449* (-0,721- -0,056)	-0,332 (-0,648-0,082)	-0,604** (-0,81- -0,266)

Fig. 2 Correlation scores: The Spearman test was used for Endotoxin vs. bacterial translocation (BT) and the Pearson test was used for the remaining variables, attending to normal distribution. Correlation was classified as moderate r=0.3-0.5, strong r=0.5-0.7, or very strong r>0.7. *p<0.05 **p<0.01; XG, xyloglucan group; NF, norfloxacin group; XG-NF, xyloglucan and norfloxacin group.

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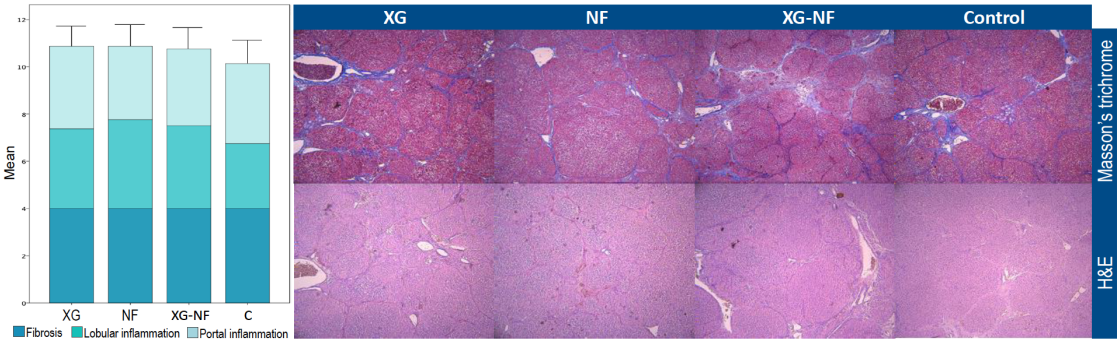

Fig. 3 Histological findings: (A) Batts and Ludwig score (0-12 points): Evaluates fibrosis, lobular inflammation, and portal inflammation on a scale of 0-4 points each. Boxes represent mean values and bars standard deviation. (B) Mason's trichrome and Hematoxilin & Eosin staining representative photomicrographs at x40 magnification. Well established cirrhosis can be identified in all groups by characteristic findings such as the expansion of portal zones, numerous fibrous bridges between portal zones (blue in Mason's trichrome) and frequent regeneration nodules encircled by these bridges (red in Mason's trichrome). XG, xyloglucan group; NF, norfloxacin group; XG-NF, xyloglucan and norfloxacin group.