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Xyloglucan: a new agent to protect the intestinal mucosa and to prevent bacterially- mediated alteration of tight junction permeability.

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Abstract

Introduction: Xyloglucan (XG) is a water-soluble hemicellulose from vascular plants, indigested by digestive enzyme. This polysaccharide has various application areas like drug-delivery technology, food technology and textile industry. It has also been suggested that it may act as a film-forming barrier distributed on the intestinal mucus layer able to protect the mucosa from chemical or bacterial aggression. However until now, no data has yet been published to confirm such hypothesis.
Aims: Our studies aimed to evaluate both in vitro and in vivo the potency of xyloglucan to prevent the bacterial toxin- induced -increase permeability and the subsequent epithelial cell bacterial invasion.
Methods: A first series of experiments performed *in vitro* on co-cultured CaCo2/Goblets cells submitted to *E. coli* inoculation, XG was added on the apical site of the bath both preventively and curatively. Changes in tight junction (TJ) permeability were measured by TEER and Lucifer yellow transfer; *E. coli* adhesion and epithelial cell invasion were counted. In a second series performed in vivo, Wistar rats received orally XG (12,5mg/kg) and 2 h. later were injected IP with LPS from *E. coli*. Jejunal strips were collected 6 hours later for in vitro TJ permeability measurement using FITC-dextran and mucosal myelo-peroxidase (MPO) activity as a marker of inflammation. In a last series, XG was given orally associated or not with gelatin or co-administered with cholera toxin (CT) into isolated jejunal loops in anesthetized rats. Evaluation of CT-induced water secretion was performed 2hours later.
Results: *In vitro,* given preventively XG (2.5mg/200ml), reduced significantly by 78% the degree of *E.coli* mucosal colonization after 30min. Added curatively, 1h after *E.coli* inoculation, XG attenuated by 87% the decrease in TEER measured 3h. later. Administered orally 2 hours before LPS, XG (12.5mg/kg) reduced significantly (P≤0.01) by 81.8% the LPS-triggered increase in permeability and subsequently by 63.2% the increase in mucosal MPO activity. When administered orally 4h earlier (12,5mg/kg) or 12h earlier with gelatin (250mg/kg), XG suppressed CT-induced water secretion. Co-administered locally with CT at dose of 0.75 and 1.25mg/loop, XG reduced (67%) or suppressed respectively, the secretory effects of CT.
Conclusions: Both in vitro and in vivo data indicate that xyloglucan has protective effects on intestinal bacterial invasion, alterations of gut permeability and CT-induced intestinal secretion reaching 12h when associated with gelatin. These data support that this compound may be of therapeutic interest in the treatment of infectious diarrhea.

Aims:

Our studies aimed to evaluate the potency of xyloglucan, a hemicellulose that occurs in the primary cell wall of all vascular plants, to prevent pathogens and bacterial toxin- induced -increase permeability and the subsequent epithelial cell bacterial invasion.

Material & &Methods:

1) In vitro studies were conducted on cultured monolayers cells (Caco2+goblet cells) submitted to E.coli infection with evaluation of intercellular permeability, transepithelial resistance and pathogen colonization.
2)In vivo influence of Cholera toxin-induced water secretion in jejunal isolated loop and E.coli LPS-induced increased tight junction permeability (FITC-Dextran 4000) and mucosal inflammation (MPO) in rats

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No conflict of interest has to be declared for SS, VT and LB

Results:

a) *In vitro* studies (Caco2 cells)

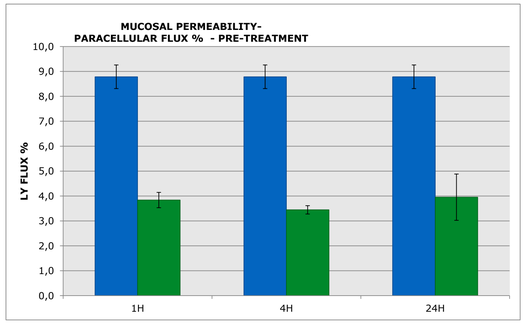


Figure 1: Change in Lucifer yellow (LY) passage from apical to basolateral site of monolayer epithelial CaCo2 cells, 30min. after *E-coli* apical application 4 or 24 h after xyloglucan (5 mg/ml) addition in the medium (apical site)

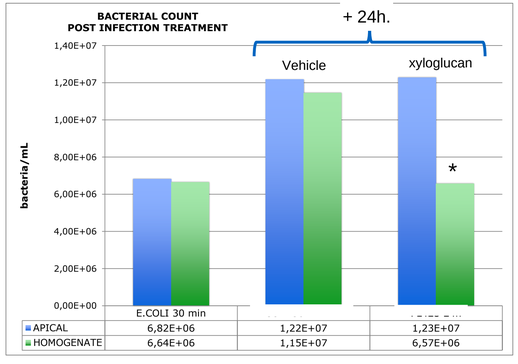


Figure 2: Twenty four hours post-infection changes in the distribution of *E.coli* density in apical and intracellular (homogenate) compartment in cultured Caco2 cells.
`Note that the presence of xyloglucan did not change the growing rate of E.coli in apical compartment while it reduced significantly (P<0.05) the degree of cell invasion.

b) *In vivo* studies (rats)

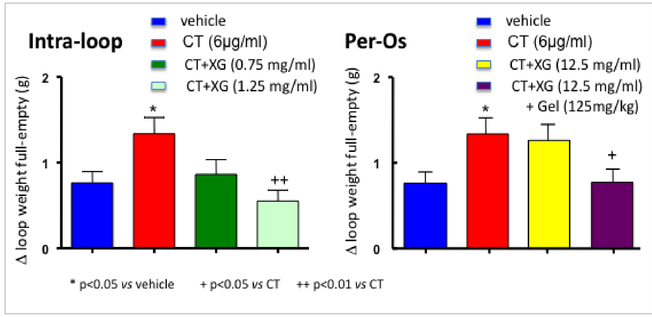


Figure 3: Comparative influence of 2 doses of xyloglucan (XG) administered directly into an isolated jejunal loop with cholera toxin (CT) or given per os , 1 hour before intraloop toxin administration on water secretion after 2 hours of CT contact (mean±SEM); n=8)

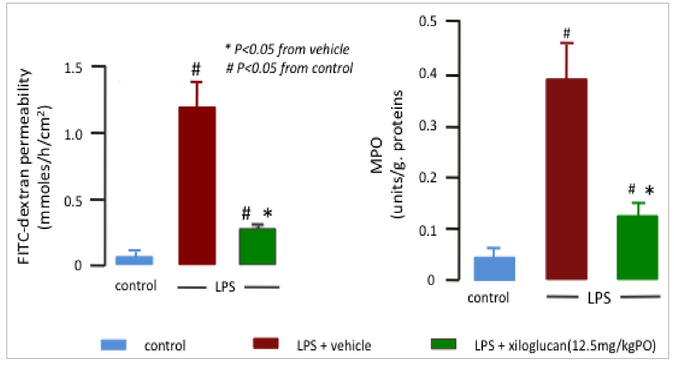
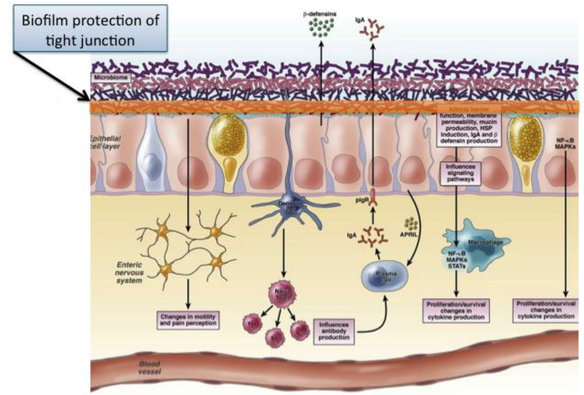


Figure 4: Comparative influence of xyloglucan (XG) administered orally (12.5mg/kg) 4 hours before IP administration of LPS (1mg/kg) on the increased in intercellular jejunal permeability (Ussing chambers) and on jejunal mucosal myeloperoxidase (MPO) activity measured 3 hours after LPS administration (mean±SEM); n=8)



(from Hollister et al. 2014)

CONCLUSIONS:

Our data obtained both *in vitro* and *in vivo* clearly demonstrate that xyloglucan administered orally is able to reduce the passage of *E.coli* into epithelial cells and basolateral space by reducing intercellular (tight junction) permeability. Similarly, *in vivo* xyloglucan given orally or locally prevent cholra toxin-induced water secretion and by suppressing the increased permeaility, limits the resulting mucosal inflammation.

We conclude that xyloglucan acts within the GI tract at mucosal level as a protective agent (bio-barrier) preventing the entry of pathogens, toxins and commensal bacteria through epithelial tight junction explaining its anti-darrheal properties.

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