

1 **Medicine food homology plant extracts alter the gut microbiota and metabolism,**
2 **alleviates polymicrobial sepsis-induced liver injury via promoting release of**
3 **interleukin-10 from M2 macrophage in mice**

4 **Significance of this study**

5 **What is already known on this subject?**

6 ► The gut-liver-immune axis describes important bidirectional communications
7 between the intestinal microbiome, liver and the mucosal immune system.

8 ► The intestinal barrier is critical for conserving normal physiology of the gut
9 microbiome. Pathogenic bacterial adherence to mucosal surfaces and barrier damage is
10 central in mucosal immune priming and may be important in the progression of liver
11 disease.

12 ► Polysaccharide, alkaloids, brass, polyphenols and saponins derived from MFH
13 plants have been shown to have antibacterial and antiinflammatory properties.

14 ► Modulation of gut microbiota using prebiotics and probiotics may improve host
15 metabolism and reduce sepsis and sepsis induced liver injury.

16 **What are the new findings?**

17 ► MFH can protect mice against sepsis and reverse sepsis-induced gut dysbiosis, leaky
18 gut, inflammation, liver injury and ABX-induced damages in CLP mice.

19 ► MFH modulates the composition of the gut microbiota, notably by enriching the gut
20 bacterium *Enterococcus* and *Lactobacillus*.

21 ► Oral treatment of CLP mice with live *L. johnsonii* bacteria prevents death, improves
22 intestinal integrity and reduces inflammation and liver injury by promoting the release
23 of IL-10 from M2 macrophages.

24 ► MFH increases the production of tryptophan (Trp) and phosphatidylcholines (PCs),
25 which are contributed to induction of M2 macrophages, by the microbiota, improving
26 gut barrier function.

27 **How might it impact on clinical practice in the foreseeable future?**

28 ► MFH represents a novel class of prebiotics to improve the treatment of sepsis
29 patients.

30 ► *E. faecalis* and *L. johnsonii* are novel probiotic bacterium that may be used to treat
31 sepsis and associated liver injury.

32 ► *L. johnsonii* promotes the release of IL-10 from M2 macrophages to alleviate sepsis
33 liver injury, which shed light on a novel mechanism of sepsis injury and suggest that
34 the therapy via targeting microbiome, IL-10 is a promising strategy to prevent sepsis
35 injury.