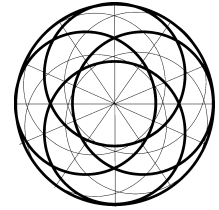




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Focus on Alternative and  
Complementary Therapies  
Volume 20(3–4) December 2015 184–186  
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DOI 10.1111/ftc.12198  
ISSN 1465-3753



### Can *Glycyrrhiza glabra* L. reduce both upper gastrointestinal tract bleeding and ventilator-associated pneumonia in intensive-care unit patients?

Gastric mucosal injury has been reported to occur during the first 24 h of hospital admission in 75–100% of intensive-care unit (ICU) patients.<sup>1</sup> Upper gastrointestinal tract bleeding (UGIB) resulting from stress-ulceration is a common outcome of such injury.<sup>2</sup> The estimated incidence of UGIB ranges from 1.5% to 6% of all ICU patients.

Although stress-ulcer prophylaxis is indicated for critical patients at high risk for UGIB, the use of these drugs can increase the likelihood of ventilator-associated pneumonia (VAP) because of the increase in gastric bacterial colonisation, gastric reflux and subsequent micro-aspiration into the lower respiratory tract.<sup>2,3</sup> Despite progress in this area, the majority of issues relating to the management of VAP and its risk factors remain unresolved in clinical practice.

Stress-ulcer prophylaxis for the prevention of UGIB can include the use of anti-reflux agents (such as sucralfate), proton pump inhibitors (PPIs) (such as pantoprazole) and histamine-2-receptor antagonists (H2RA) (such as ranitidine).<sup>4</sup> Sucralfate covers the gastric mucosa and prevents the movement of bacteria towards the pharynx and lungs. Considering that gastric acid production is not inhibited with the use of sucralfate, patients receiving sucralfate therapy are less likely to experience aspiration pneumonia relative to other agents.<sup>4</sup> Although the risk of aspiration and VAP is reduced following the use of sucralfate, the development of UGIB is relatively higher.<sup>5,6</sup>

Moderate to high quality evidence supports the use of acid-inhibiting agents over sucralfate in the prevention of UGIB.<sup>5</sup> However, the administration of PPIs and H2RAs as acid inhibitors can facilitate the colonisation of bacteria in the stomach by inhibiting the secretion of gastric acid. This can create a source for bacterial micro-aspiration into the lungs, which increases the risk of VAP.<sup>4</sup>

Given the increased risk of pneumonia and/or UGIB with these aforementioned medications,

there is a need for appropriate adjuvant agents that can reduce the risk of VAP and UGIB concomitantly and with minimal complication. *Glycyrrhiza glabra* L. (licorice) maybe one such agent.

*Glycyrrhiza glabra* is a traditional medicinal herb that grows in many parts of the world.<sup>7</sup> Glycyrrhizin (glycyrrhizic acid), glabridin, glabrene, glabrol, licoflavonol, glycyrol and licoricone are some of the compounds isolated from *G. glabra*.<sup>7</sup> In medicine, *G. glabra* root has commonly been used to treat gastric and duodenal ulceration as an alternative to bismuth. The root has been shown to have a protective role against acid and pepsin secretion by covering the site of the lesion and promoting mucous secretion.<sup>8,9</sup>

Szweda *et al.* evaluated the muco-protective effects of *G. glabra* (i.e. liquid alcohol extract) on canine colonic mucosa following the administration of NSAIDs at an oral dose of 50 mg every 24 h in dogs weighing up to 10 kg.<sup>10</sup> Their results showed a reduction in the severity of NSAID-induced mucosal damage after prophylactic treatment with *G. glabra*. Sancar *et al.* achieved the same results.<sup>11</sup> Moreover, Ligha *et al.* demonstrated that *G. glabra* had protective effects against alcohol-induced gastric mucosa damage by increasing mucus production, preventing mucus depletion and/or inhibiting lipid peroxidation.<sup>12</sup> *Glycyrrhiza glabra* thus offers a natural approach for the management of gastro-oesophageal reflux disease and related disorders.<sup>13</sup>

To the best of our knowledge, there are few pre-clinical and clinical studies that have evaluated the anti-reflux properties of *G. glabra* extract. The antibacterial activity of *G. glabra* is well known, however. Several *in vitro* studies have shown that many compounds isolated from the extract of *G. glabra* have antibacterial effects against methicillin sensitive *Staphylococcus aureus* (MSSA), methicillin resistant *S. aureus* (MRSA), *Mycobacterium tuberculosis* and *Helicobacter pylori*.<sup>7,14,15</sup> Animal studies also reveal a decrease in mortality and viral activity after using *G. glabra* against *Herpes simplex*, HIV-1, severe acute respiratory syndrome (SARS)-related coronavirus (SARS-CoV), respiratory syncytial virus (RSV), arboviruses, vesicular stomatitis virus (VSV) and influenza A virus pneumonia.<sup>16</sup>

Considering that selective digestive tract decontamination (SDD) is an important measure for VAP prevention in the ICU patient,<sup>17</sup> the antimicrobial properties of *G. glabra* might be beneficial in reducing the risk of VAP in critically ill patients.

Recently, an *in-vitro* study demonstrated that *G. glabra* provides a high grade of protection against alpha-haemolysin-mediated alveolar epithelial cell injury and can relieve the pulmonary inflammatory reaction caused by *S. aureus*-induced pneumonia in a murine model. The authors proposed that *G. glabra* may potentially be useful for the treatment of *S. aureus*-induced pneumonia when used in combination with beta-lactam antibiotics.<sup>18</sup>

In summary, it seems that *G. glabra* might reduce the risk of UGIB and also prevent the development of VAP through antibacterial, anti-reflux, anti-peptic ulceration and anti-inflammatory effects in ICU intubated patients. Furthermore, *G. glabra* has a low-cost, high tolerability and minimal side-effects. We recommend further *in-vitro* research in this field. Also, with respect to the efficacy of *G. glabra*, and its related compounds as an adjuvant therapy in clinical medicine, this has yet to be proven; thus, we suggest that double-blind, randomised controlled studies of *G. glabra*, with the appropriate dosage and duration of treatment, be conducted in patients undergoing mechanical ventilation in the ICU with close monitoring of VAP and UGIB occurrence.

**Conflict of interest** None declared.

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