
Treatment of antibiotic associated diarrhea

A common side effect of antibiotics is diarrhea. Diarrhea causes the increase in length of stay in Healthcare facilities and increase the cost of treatment. As a cause of diarrhea, CDI, in many developed countries has become the major issue. There has been an increase of CDI incident and severity since the discovery of *C. difficile* in the 1970s. Recent reports show a mild increase in incident, severity and mortality albeit the huge progress in managing and treating CDI (Al-Jashaami and DuPont 2016). In USA, CDI has become the most frequent infection reported to the health-care organisation and its outbreak is due to more virulent strains that cause severe disease (Gerding, Muto et al. 2008). Based on data from US death certificates, the CDI mortality rate was 14000 in 2007, 29000 in 2011, and 44500 in 2014 (Hopkins and Wilson 2017). In addition, the cost of treatment of CDI and hospitalisation is significant. Treatment of CDI is ranged between US\$2871 to US\$4846 in the USA and US\$5243 to US\$8570 outside the USA which only cover the medication and laboratory without the hospitalisation which is the biggest cost driver (Ghantoji, Sail et al. 2010). Although the diagnosis and treatment have advanced in the past two decades, yet the prevention of CDI has remained a challenged especially in healthcare facilities. Despite the use of antibiotics for treating CDI, other potential treatment factors have been explored such as the use of probiotic bacteria.

Probiotics are live organisms that, when administered in adequate dosage, can be beneficial to host by restoring the normal level of bacteria in the gut. Probiotics is another advance approach in hindering the development of CDI. Since antibiotic treatment can disrupt the natural colonic microbiota, probiotics treatment prevents the disruption of the microbiome and that could prevent CDI. A study showed that administering lactobacillus to the hospitalised patients on antibiotics resulted in a reduction in diarrheal symptoms and reduction of CDI risk (Avila, Avila et al. 2016). Probiotics can be used as a chaser treatment on patients after a full course of anti-CDI antibiotics. Some probiotics have immunorectavie effect in-which administration them can increase the IgA level in the gut and prevent the production of proinflammatory cytokines such as interleukin 8 (Buts, Bernasconi et al. 1990, Dahan, Dalmaso et al. 2003).

Bacillus species have shown to producing antimicrobial agents that can inhibit some pathogens i.e. the supernatant of *B. subtilis* (strain name: URID 12.1) showed antimicrobial activity by inhibited the growth of multidrug resistant strains of *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus pyogenes* and *Enterococcus faecalis* (Chalasani, Dhanarajan et al. 2015). Bacteriocin-like substance from *B. subtilis* has been shown to inhibit different clinical bacteria such as *Salmonella typhi* that causes typhoid (Boottanun, Potisap et al. 2017). The antibiotics secreted from *B. megaterium* showed activity against *Leuconostoc mesenteroides* (strain: VKPM B-4177), that is resistant to glycopeptide antibiotics, and also gram-negative

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bacteria *Pseudomonas aeruginosa* (Malanicheva, Kozlov et al. 2012). *B. amyloliquefaciens* (strain FZB42) can produce a dipeptide protein called Bacilysin that can suppress the growth of *E. amylovora*. *B. amyloliquefaciens* can also kill *Burkholderia pseudomallei*, which is the causative agent for melioidosis, via the secondary metabolites (Boottanun, Potisap et al. 2017).

The fact that *Bacillus* species inhibit many pathogens by producing antimicrobial agents raises the question of whether there would be any activity by these species that can inhibit the growth of *C. difficile* and help to prevent CDI. Since most of the *Bacillus* species has been recognised safe for human consumption, if they have any activity against *C. difficile*, it could be used as an effective potential treatment for CDI. In this chapter, the antimicrobial activity of different *Bacillus* species against *C. difficile* was investigated.

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