isolates. The carbapenems had high affinity for all PBPs in a penicillin-susceptible isolate but had reduced binding affinity, particularly to PBP2x and PBP2b, in a penicillin-resistant isolate.

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Transparency declarations

T. A. D., W. S., K. B. and R. K. F. own shares in Johnson & Johnson and are employees of Johnson & Johnson Pharmaceutical Research and Development, L.L.C.

References


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Red bayberry extract inhibits growth and virulence gene expression of the human pathogen Vibrio cholerae

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Sir,

Today, when most clinically relevant bacteria are displaying increasing antibiotic resistance, discovery of novel and cost-efficient antimicrobial compounds is increasingly critical. Vibrio cholerae is a Gram-negative bacterium that is the causative agent for the severe diarrhoeal disease cholera, which still remains a global killer mainly in the developing countries.1 In addition to causing significant mortality, V. cholerae also causes high rates of morbidity, which imposes a severe social and economic burden on affected communities that are often already lacking in medical and economic resources.

Red bayberry (Myrica rubra) is a small to medium-sized tree growing in East and Southeast Asia. The plant is used in Chinese traditional medicine for treatment of cholera and other diarrhoeal diseases.2 To investigate the biochemical mechanism behind this activity, we extracted compounds from bayberry fruits using 50% ethanol, followed by drying with a rotary evaporator. The pellet was then resuspended in water for a final concentration of 1 g of fruit extract/mL, and the pH of the mixture was adjusted to 7.0. We then added various amount of this bayberry extract to the mid-log cultures of a V. cholerae El Tor strain and incubated these cultures for 2 h. The number of surviving bacteria was determined by plating on LB plates. High concentrations of the extract killed V. cholerae completely, while low concentrations inhibited bacterial growth, MIC of 125 g/L (data not shown and Figure 1a). We then assayed for the production of two major virulence determinants, that of the toxin-coregulated pilus (TCP) by western blot and of cholera toxin (CT) production by ELISA, in the presence of non-inhibitory concentrations of the bayberry extract. TCP is thought to play a role in early attachment of vibrios to the intestinal epithelium and is required for intestinal colonization in an infant mouse model of cholera, as well as for cholera in humans.3 Figure 1(b) shows that 10 mg/mL bayberry extract reduced both TcpA and CT production, while higher concentrations of extract completely inhibited virulence factor production. The inhibition of virulence gene expression at low concentrations and the bactericidal effect at high concentrations led us to test whether the bayberry extract can reduce V. cholerae colonization in an infant mouse model. Normally, ~105 V. cholerae could be recovered from one mouse intestine 24 h post-infection. When 100 mg of bayberry extract was co-inoculated with bacteria, the number of colonized bacteria was significantly reduced (Figure 1c, left-hand panel). We also examined whether the extract could reduce infection if administered after colonization had already been established in the infant mouse. We found that delayed administration of extracts 12 h after inoculation with V. cholerae still reduced the recovery of V. cholerae by over 1000-fold relative to bacteria recovered from untreated V. cholerae-infected infant mice (Figure 1c, right-hand panel). These data suggest that the bayberry extract could have utility even after the establishment of V. cholerae in the gut.
In this study, we investigated the molecular mechanism behind bayberry treatment of cholera described in ancient Chinese medicine. We found that an extract derived from a simple and rapid extraction of bayberry fruits could repress \textit{V. cholerae} virulence gene expression at low concentrations and inhibit \textit{V. cholerae} growth at high concentrations. Intriguingly, this bayberry extract did not inhibit or kill many non-pathogenic bacteria tested, including \textit{Escherichia coli} and \textit{Bacillus subtilis} (data not shown). The narrow-spectrum bactericidal activity of the bayberry extract may thus preserve normal intestinal flora during treatment. Thus far, there has been little success in finding cheap and effective treatments for poverty-associated infectious diseases like cholera. For example, although Hung \textit{et al.}\textsuperscript{,4} reported a compound that can specifically inhibit \textit{V. cholerae} virulence gene expression \textit{in vitro} and \textit{in vivo}, such compounds must be artificially synthesized. Further study is necessary to reveal the exact nature of bayberry extract inhibition of \textit{V. cholerae} infection, but consumption of bayberry fruits or fruit extracts may prove to be a cheap alternative therapy for cholera in many developing countries.

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\section*{Transparency declarations}

None to declare.

\section*{Supplementary data}

A colour version of Figure 1 is available as Supplementary data at \textit{JAC} Online (http://jac.oxfordjournals.org/).

\section*{References}

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\section*{Thermostable nuclease: a study of clinical impact}

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Keywords: bacteraemia, \textit{Staphylococcus aureus}, rapid diagnosis

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Sir,

Bacteraemia due to \textit{Staphylococcus aureus} is associated with a high morbidity and mortality. Early detection and treatment is critical for successful management. Unfortunately, coagulase-negative staphylococci (CoNS) are the most frequent isolates grown from blood cultures, many of which are considered skin contaminants. A test that rapidly and accurately discriminates the two would potentially allow earlier treatment of \textit{S. aureus}, while reducing unnecessary antimicrobial use. Thermostable nuclease (TSN) is a rapid test (requiring 2–4 h)