Abstract

Managing the deregulated host response to infection remains a major challenge in sepsis care. Chinese treatment guideline recommends adding XueBiJing, a fve-herb medicine, to antibiotic-based sepsis care. Although adding XueBiJing further reduced 28-day mortality via modulating the host response, pharmacokinetic herb-drug interaction is a widely recognized issue that needs to be studied. Building on our earlier systematic chemical and human pharmacokinetic investigations of XueBiJing, we evaluated the degree of pharmacokinetic compatibility for XueBiJing/antibiotic combination based on mechanistic evidence of interaction risk. Considering both XueBiJing 5e $5 \circ$

 \mathbf{K} ..., \mathbf{K} eB J. - A ... b. - c C ... b. a... d. ... e a- Se. - P. a. ac ... e.c.c. ... a.b.

D ... ac, b, a... d ... e a , a... c a f ... fac... a d, ea e, ca , a e d, ... c . ec a ... f ac... a d e e e, a ced ... a ac d, a c e ec. T e, e, c ... e a e c be e , a ... d de ee f, a, ac ... e c c ... a b ... (PKC), de ed a ... e c -ad ... e ed d \rightarrow PKC, de ed a ab e ce. f ... e ... a a a eab e , a ... a c ... e c (PK) d ... e ac... a ca ead ... dec ea ed d e cac ... c ea ed d ... c .

 $Se_{a_1,a_2,a_3,a_4}, fe_{a_1,a_2,a_3,a_4} a_{a_1,a_2,a_3} c_{a_1,a_2,a_3} c_{a_2,a_3} ed b a de e a ed$ $(\ldots, \ldots, e_{a_1}, \ldots, e_{a_1}, \ldots, fec_{a_n}, 4. Beca_{a_n} e_{a_n} fec_{a_n} ca_{a_n} e_{a_n} e_{a_n}$ $, e_1, \ldots, e_n, \ldots, e_n, \ldots, e_n, \ldots, e_n, \ldots, a_n, \ldots, a_n, \ldots, f_n a_n, \ldots, a_n$ $a_{1} \circ a_{2} \circ b_{2} \circ a_{3} \circ c_{4} \circ c_{4} \circ e_{2} \circ a_{2} \circ e_{2} \circ e_{2} \circ a_{3} \circ c_{4} \circ e_{2} \circ a_{3} \circ a_{4} \circ e_{2} \circ a_{3} \circ a_{4} \circ e_{2} \circ a_{3} \circ a_{4} \circ e_{2} \circ a_{3} \circ e_{2} \circ a_{4} \circ e_{2} \circ e_{2$ cale. H e e, e e a e, cce, f ... ea, e ..., f, e, ..., a ... fec..., $(\mathbf{e}_1, \mathbf{e}_2, \mathbf{e}_1, \mathbf{e}_2, \mathbf{e}_1, \mathbf{e}_2, \mathbf{e}_1, \mathbf{e}_2, \mathbf{e}_1, \mathbf{e}_2, \mathbf{e}_3, \mathbf{e}_1, \mathbf{e}_2, \mathbf{e}_3, \mathbf{e}_1, \mathbf{e}_2, \mathbf{e}_3, \mathbf{e$ a d . a ed c ... , ca . c . e . a . c ... He ce, a e a_{11} ... , e (a,b) = (a,e) + (a,b) + (a,b $, a \ e \ bee \ , \ ade \ldots \ , \ de \ , \ a \ d \ , \ \ , \ e \ , a \ , \ , \ , \ , \ , \ , \ f \ , \ e \ , \ , \ ,$ $e_{i} \mathrel{,} \ldots \mathrel{,} e_{i} \mathrel{,} \ldots \mathrel{,} c_{i} \mathrel{,} \ldots \mathrel{,} c_{i} \mathrel{a} \mathrel{ac} e_{i} \mathrel{,} zed \mathrel{b} \mathrel{,} e_{i} \mathrel{ab} \mathrel{,} da \mathrel{,} \ldots \mathrel{,} a \mathrel{e} \mathrel{,} \ldots \mathrel{,} e_{i}$ $(\mathbf{c}_1, \ldots, \mathbf{e}_{n-1}, \mathbf{e}$ $c_1, \ldots, e_i, e_i, \ldots, e_i, c_i, a_i, \ldots, a_i, \ldots, a_i, \ldots, e_i, e_i, e_i, a_i, \ldots, a_i, \ldots, e_i, a_i, \ldots, a$ $ea(c,-f) = (1,1), \quad ac(-1), \quad e(a,-e(-1),-d) = a(e(-1), \quad e(-1),-e(-1), \quad e(-1),-e(-1), \quad e(-1),-e(-1), \quad e(-1),-e(-1),-e(-1), \quad e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1),-e(-1$ $C_{c}\ldots \ a \ F_{c} \ , \ d \ a \ d \ D_{c} \ \ Ad \ \ldots \ , \ldots \ a \ \ldots \) \ , \ ec \ \ ca \ \ f \ \ldots \ ea \ \ ea \ \ f$ $, \ e_{\mathcal{F},\mathcal{F}} \ a \ d_{\mathcal{F}} \ = \ a \ d_{\mathcal{F}} \ f \ , \ c_{\mathcal{F},\mathcal{F}} \ , \ d_{\mathcal{F},\mathcal{F}} \ e \ [3], I_{\mathcal{F},\mathcal{F}} \ a \ da \ d \ zed$ $\dots \ a \ e \ , \ , \ , \ e c \ , \ , \ , \ e \ a \ e d \ f \ , \ a \ e \ , \ e \ b \ c \ , \ b \ , \ a \ , \ ,$ $(C_{c} a \dots), A e_{c} ca_{d} \dots e_{d}), a dSa a \dots za$

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b. a a ab ef d ... e ac..., f. d ed X eB J. e e b a ed f. ... ea e e e a c ... e e b a ed c e [5]. L e a e. ... a e f ed de f a b c edf e... ca e. C. a a d b b a f a b e a d e a a ac e c /d... a d d e ac... ab e, a e a f a ... e a c... ab e f X eB J. a d e a ed e b a c ... d . D e e a e c ... d e e e