

Supporting Information

Antimicrobial Structure-activity Relationships of Cannabinoids

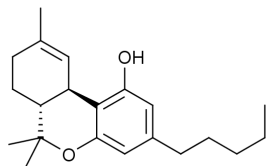
John A. Karas, Labell J. M. Wong, Olivia K. A. Paulin, Amna C. Mazeah,
Maytham H. Hussein, Jian Li, Tony Velkov^{*}

Antibacterial activity of Δ^9 -tetrahydrocannabinol and cannabidiol

van Klinger, B., Ham, M. T.,

Antonie Van Leeuwenhoek, 1976, 42, 9-12.

MIC reported in $\mu\text{g/mL}$



1. Δ^9 -tetrahydrocannabinol

Nutrient broth agar

S. aureus (4 strains) = 2-5

S. pyogenes (1 strain) = 5

S. milleri (1 strain) = 2

S. faecalis (1 strain) = 5

E. coli (4 strains) > 100

S. typhi (1 strain) > 100

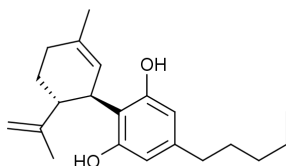
P. vulgaris (1 strain) > 100

Horse blood agar

S. aureus (4 strains) = 20-50

S. pyogenes (1 strain) = 50

S. milleri (1 strain) = 50



2. Cannabidiol

Nutrient broth agar

S. aureus (4 strains) = 1-5

S. pyogenes (1 strain) = 2

S. milleri (1 strain) = 1

S. faecalis (1 strain) = 5

E. coli (4 strains) > 100

S. typhi (1 strain) > 100

P. vulgaris (1 strain) > 100

Horse blood agar

S. aureus (4 strains) = 20-50

S. pyogenes (1 strain) = 50

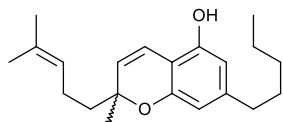
S. milleri (1 strain) = 50

Biological Activity of Cannabichromene, its Homologs and Isomers

Turner, C. E., Elsohly, M. A.,

J. Clin. Pharmacol., **1981**, 21, 283S–291S.

MIC reported in $\mu\text{g/mL}$



3. Cannabichromene (IV)

B. subtilis 24 h = 0.39

B. subtilis 48 h = 0.78

S. aureus 24 h = 1.56

S. aureus 48 h = 1.56

M. smegmatis 24 h = 12.5

M. smegmatis 48 h = 25.0

C. albicans 48 h = NT

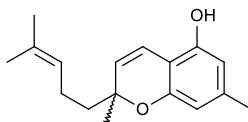
C. albicans 72 h = NT

S. cerevisiae 48 h = 25

S. cerevisiae 72 h = 50

T. mentagrophytes 48 h = 25

T. mentagrophytes 72 h = 50



4. Cannabichromene-C₁ (V)

B. subtilis 24 h = 3.12

B. subtilis 48 h = 3.12

S. aureus 24 h = 3.12

S. aureus 48 h = 3.12

M. smegmatis 24 h = 3.12

M. smegmatis 48 h = 6.25

C. albicans 48 h = NT

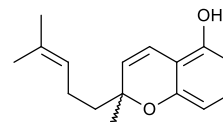
C. albicans 72 h = NT

S. cerevisiae 48 h = 6.25

S. cerevisiae 72 h = 12.5

T. mentagrophytes 48 h = 6.25

T. mentagrophytes 72 h = 6.25



5. Cannabichromene-C₀ (VI)

B. subtilis 24 h = 6.25

B. subtilis 48 h = 12.5

S. aureus 24 h = 12.5

S. aureus 48 h = 12.5

M. smegmatis 24 h = 12.5

M. smegmatis 48 h = 12.5

C. albicans 48 h = 50

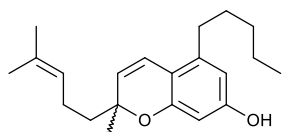
C. albicans 72 h = 50

S. cerevisiae 48 h = 25

S. cerevisiae 72 h = 25

T. mentagrophytes 48 h = 25

T. mentagrophytes 72 h = 25



6. Isocannabichromene (VII)

B. subtilis 24 h = 0.78

B. subtilis 48 h = 3.12

S. aureus 24 h = NT

S. aureus 48 h = NT

M. smegmatis 24 h = 25.0

M. smegmatis 48 h = 25.0

C. albicans 48 h = 50

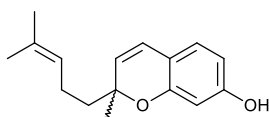
C. albicans 72 h = 100

S. cerevisiae 48 h = NT

S. cerevisiae 72 h = NT

T. mentagrophytes 48 h = NT

T. mentagrophytes 72 h = NT



7. Isocannabichromene-C₀ (VIII)

B. subtilis 24 h = 6.25

B. subtilis 48 h = 6.25

S. aureus 24 h = 12.5

S. aureus 48 h = 12.5

M. smegmatis 24 h = 12.5

M. smegmatis 48 h = 12.5

C. albicans 48 h = 12.5

C. albicans 72 h = 25

S. cerevisiae 48 h = NT

S. cerevisiae 72 h = NT

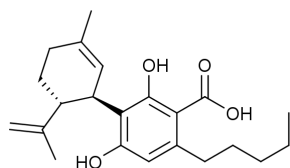
T. mentagrophytes 48 h = 6.25

T. mentagrophytes 72 h = 6.25

Antibacterial Cannabinoids from *Cannabis sativa*: A Structure-Activity Study

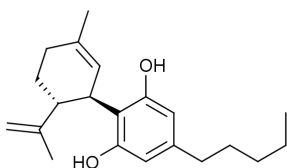
Appendino, G., Gibbons, S., Giana, A., Pagani, A., Grassi, G., Stavri, M., Smith, E., Mukhlesur Rahman, M.,
J. Nat. Prod., **2008**, 71, 1427–1430.

MIC reported in $\mu\text{g/mL}$



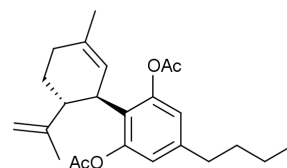
8. Analog 1a

S. aureus SA-1199B = 2
S. aureus RN-4220 = 2
S. aureus XU212 = 2
S. aureus ATCC25923 = 2
S. aureus EMRSA-15 = 2
S. aureus EMRSA-16 = 2



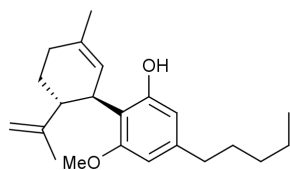
9. Analog 1b

S. aureus SA-1199B = 1
S. aureus RN-4220 = 1
S. aureus XU212 = 1
S. aureus ATCC25923 = 0.5
S. aureus EMRSA-15 = 1
S. aureus EMRSA-16 = 1



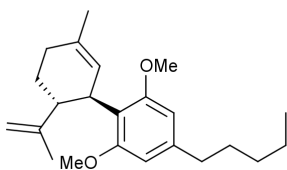
10. Analog 1c

S. aureus SA-1199B > 128
S. aureus RN-4220 > 128
S. aureus XU212 > 128
S. aureus ATCC25923 > 128
S. aureus EMRSA-15 > 128
S. aureus EMRSA-16 > 128



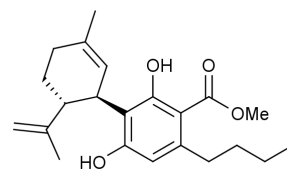
11. Analog 1d

S. aureus SA-1199B > 128
S. aureus RN-4220 > 128
S. aureus XU212 > 128
S. aureus ATCC25923 > 128
S. aureus EMRSA-15 > 128
S. aureus EMRSA-16 > 128



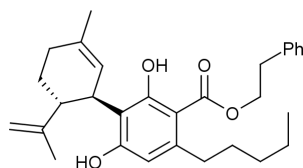
12. Analog 1e

S. aureus SA-1199B > 128
S. aureus RN-4220 > 128
S. aureus XU212 > 128
S. aureus ATCC25923 > 128
S. aureus EMRSA-15 > 128
S. aureus EMRSA-16 > 128



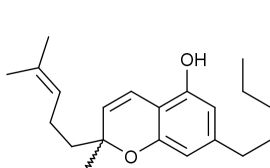
13. Analog 1f

S. aureus SA-1199B > 128
S. aureus RN-4220 > 128
S. aureus XU212 > 128
S. aureus ATCC25923 > 128
S. aureus EMRSA-15 > 128
S. aureus EMRSA-16 > 128



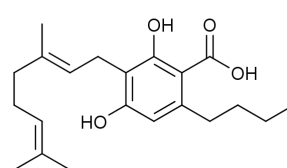
14. Analog 1g

S. aureus SA-1199B > 128
S. aureus RN-4220 > 128
S. aureus XU212 = > 128
S. aureus ATCC25923 > 128
S. aureus EMRSA-15 > 128
S. aureus EMRSA-16 > 128



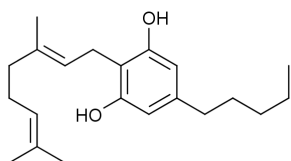
15. Analog 2

S. aureus SA-1199B = 2
S. aureus RN-4220 = 2
S. aureus XU212 = 1
S. aureus ATCC25923 = 2
S. aureus EMRSA-15 = 2
S. aureus EMRSA-16 = 2



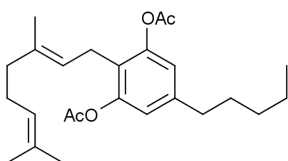
16. Analog 3a

S. aureus SA-1199B = 4
S. aureus RN-4220 = 2
S. aureus XU212 = 4
S. aureus ATCC25923 = 4
S. aureus EMRSA-15 = 2
S. aureus EMRSA-16 = 4



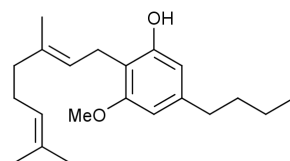
17. Analog 3b

S. aureus SA-1199B = 1
S. aureus RN-4220 = 1
S. aureus XU212 = 1
S. aureus ATCC25923 = 1
S. aureus EMRSA-15 = 2
S. aureus EMRSA-16 = 1



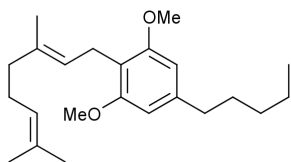
18. Analog 3c

S. aureus SA-1199B > 128
S. aureus RN-4220 > 128
S. aureus XU212 > 128
S. aureus ATCC25923 > 128
S. aureus EMRSA-15 > 128
S. aureus EMRSA-16 > 128



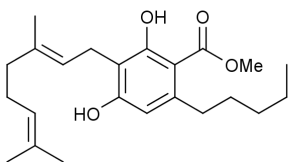
19. Analog 3d

S. aureus SA-1199B > 128
S. aureus RN-4220 > 128
S. aureus XU212 > 128
S. aureus ATCC25923 > 128
S. aureus EMRSA-15 > 128
S. aureus EMRSA-16 > 128



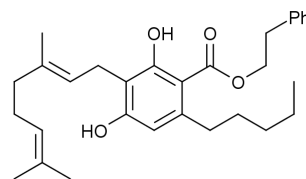
20. Analog 3e

S. aureus SA-1199B > 128
S. aureus RN-4220 > 128
S. aureus XU212 > 128
S. aureus ATCC25923 > 128
S. aureus EMRSA-15 > 128
S. aureus EMRSA-16 > 128



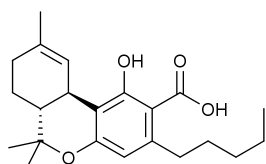
21. Analog 3f

S. aureus SA-1199B = 64
S. aureus RN-4220 = ND
S. aureus XU212 = 64
S. aureus ATCC25923 = ND
S. aureus EMRSA-15 = ND
S. aureus EMRSA-16 = ND



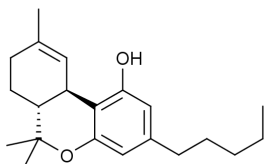
22. Analog 3g

S. aureus SA-1199B > 128
S. aureus RN-4220 > 128
S. aureus XU212 > 128
S. aureus ATCC25923 > 128
S. aureus EMRSA-15 > 128
S. aureus EMRSA-16 > 128



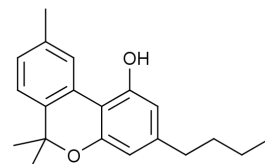
23. Analog 4a

S. aureus SA-1199B = 8
S. aureus RN-4220 = 4
S. aureus XU212 = 8
S. aureus ATCC25923 = 4
S. aureus EMRSA-15 = 8
S. aureus EMRSA-16 = 4



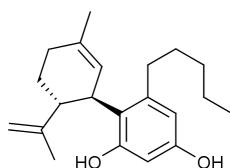
24. Analog 4b

S. aureus SA-1199B = 2
S. aureus RN-4220 = 1
S. aureus XU212 = 1
S. aureus ATCC25923 = 1
S. aureus EMRSA-15 = 2
S. aureus EMRSA-16 = 0.5



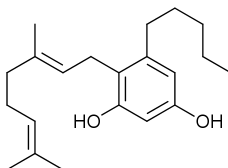
25. Analog 5

S. aureus SA-1199B = 1
S. aureus RN-4220 = 1
S. aureus XU212 = 1
S. aureus ATCC25923 = 1
S. aureus EMRSA-15 = 1
S. aureus EMRSA-16 = ND



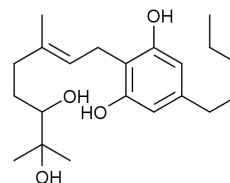
26. Analog 6

S. aureus SA-1199B = 1
S. aureus RN-4220 = 1
S. aureus XU212 = 1
S. aureus ATCC25923 = 1
S. aureus EMRSA-15 = 1
S. aureus EMRSA-16 = 1



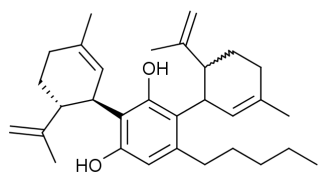
27. Analog 7

S. aureus SA-1199B = 2
S. aureus RN-4220 = 1
S. aureus XU212 = 0.5
S. aureus ATCC25923 = 1
S. aureus EMRSA-15 = 2
S. aureus EMRSA-16 = ND



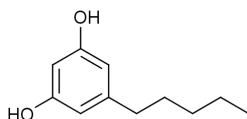
28. Analog 8

S. aureus SA-1199B = 32
S. aureus RN-4220 = 32
S. aureus XU212 = 16
S. aureus ATCC25923 = 16
S. aureus EMRSA-15 = 16
S. aureus EMRSA-16 = 32



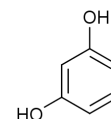
29. Analogue 9

S. aureus SA-1199B > 128
S. aureus RN-4220 > 128
S. aureus XU212 > 128
S. aureus ATCC25923 > 128
S. aureus EMRSA-15 > 128
S. aureus EMRSA-16 > 128



30. Analogue 10

S. aureus SA-1199B = 64
S. aureus RN-4220 = 64
S. aureus XU212 = 64
S. aureus ATCC25923 = 128
S. aureus EMRSA-15 = 64
S. aureus EMRSA-16 = 64



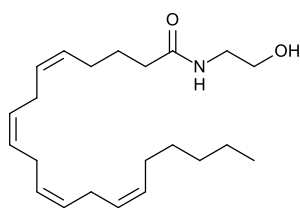
31. Analogue 11

S. aureus SA-1199B > 256
S. aureus RN-4220 > 256
S. aureus XU212 > 256
S. aureus ATCC25923 > 256
S. aureus EMRSA-15 > 256
S. aureus EMRSA-16 > 256

Antimicrobial potential of endocannabinoid and endocannabinoid-like compounds against methicillin-resistant *Staphylococcus aureus*

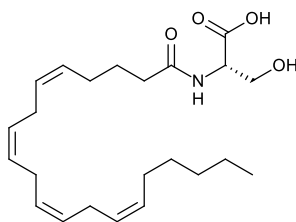
Feldman, M., Smoum, R., Mechoulam, R., Steinberg, D.,
Sci. Rep., **2018**, 8, 17696.

MIC reported in µg/mL



32. Anandamide

MRSA 33592 > 256
 MRSA CI > 256
 MRSA 43300 > 256



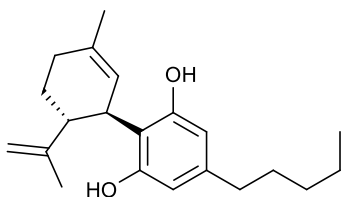
33. Arachidonoyl serine

MRSA 33592 = 32
 MRSA CI > 256
 MRSA 43300 128

Cannabidiol is an effective helper compound in combination with bacitracin to kill Gram-positive bacteria

Wassmann, C. S., Højrup, P., Klitgaard, J. K.,
Sci. Rep., **2020** 10, 4112.

MIC reported in µg/mL



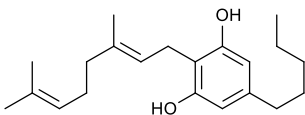
34. Cannabidiol

MRSA USA300 FPR3757 = 4
E. faecalis (13–327129) = 8
L. monocytogenes (EGD) = 4
MRSE (933010 3F-16 b4) = 4

Uncovering the Hidden Antibiotic Potential of Cannabis

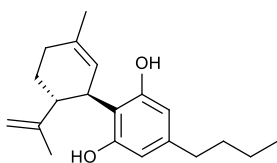
Farha, M. A., El-Halfawy, O. M., Gale R. T., MacNair, C. R., Carfrae, L. A., Zhang, X., Jentsch, N. G.,
Magolan, J., Brown, E. D.,
ACS Infect. Dis., **2020**, 6, 338–346.

MIC reported in µg/mL



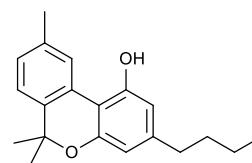
35. Cannabigerol

MRSA USA300 = 2
E. coli > 128



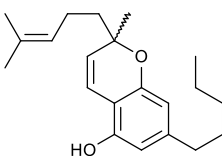
36. Cannabidiol

MRSA USA300 = 2
E. coli > 128



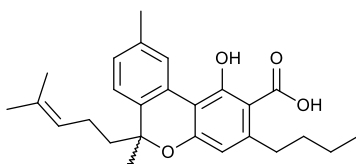
37. Cannabinol

MRSA USA300 = 2
E. coli > 128



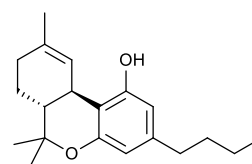
38. Cannabichromene

MRSA USA300 = 8
E. coli > 128



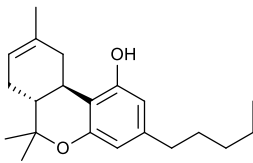
39. Cannabichromenic acid

MRSA USA300 = 2
E. coli > 128

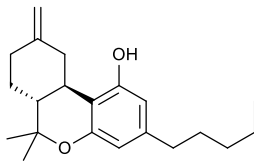


40. (-)-Δ⁹-Tetrahydrocannabinol

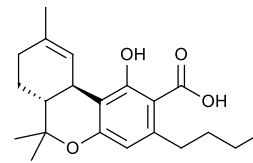
MRSA USA300 = 2
E. coli > 128



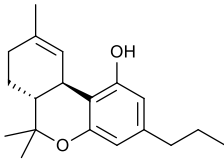
41. (-)Δ⁸-Tetrahydrocannabinol
 MRSA USA300 = 2
E. coli > 128



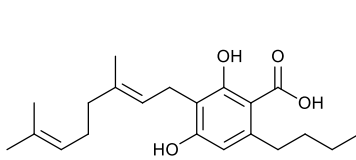
42. exo-Tetrahydrocannabinol
 MRSA USA300 = 2
E. coli > 128



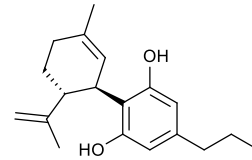
43. (-)Δ⁹-Tetrahydrocannabinol acid A
 MRSA USA300 = 4
E. coli > 128



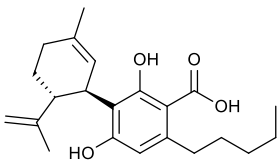
44. Δ⁹-Tetrahydrocannabivarin
 MRSA USA300 = 4
E. coli > 128



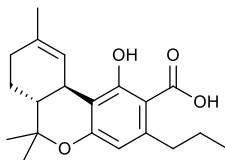
45. Cannabigerolic acid
 MRSA USA300 = 4
E. coli > 128



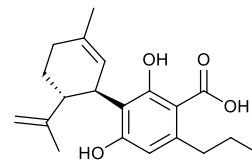
46. Cannabidivarin
 MRSA USA300 = 8
E. coli > 128



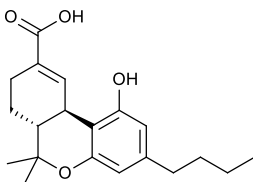
47. Cannabidiolic acid
 MRSA USA300 = 16
E. coli > 128



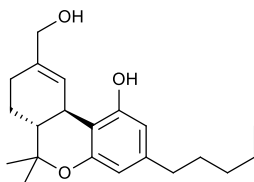
48. Tetrahydrocannabivarinic acid
 MRSA USA300 = 16
E. coli > 128



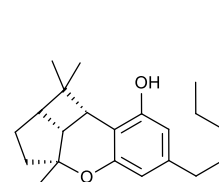
49. Cannabidivarinic acid
 MRSA USA300 = 32
E. coli > 128



50. (±) 11-nor-9-carboxy-Δ⁹-THC
 MRSA USA300 > 32
E. coli > 128



51. (±) 11-hydroxy-Δ⁹-THC
 MRSA USA300 > 32
E. coli > 128



52. Cannabicyclol
 MRSA USA300 > 32
E. coli > 128