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Repurposing cannabidiol (CBD) as novel antimicrobial candidate targeting methicillin-resistant and vancomycin-intermediate Staphylococcus aureus

Povilas Kavaliauskas[1,2,3], Rūta Petraitienė[1,2], Vida Budrienė[4], Arūnas Jonušas[4], Lina Mlečkė[4], Juozas Sakalauskas[4], Ramunė Grigalevičiūtė[3], and Vidmantas Petraitis[1,2,3]

[1] Transplantation-Oncology Infectious Diseases Program, Division of Infectious Diseases, Department of Medicine, Weill Cornell Medicine of Cornell University, New York, New York, USA; [2] Institute of Infectious Diseases and Pathogenic Microbiology, Prienai, Lithuania; [3] Biological Research Center, Lithuanian University of Health Sciences, Kaunas, Lithuania; [4] Biosyyd, Kaunas, Lithuania

Weill Cornell Medicine
Povilas Kavaliauskas
Phone:1-646-946-8841
Email: pok4001@med.cornell.edu

Weill Cornell Medicine

Biosyyd.

INTRODUCTION

Infections caused by methicillin-resistant Staphylococcus aureus (MRSA) are responsible for high morbidity and mortality worldwide. The horizontal acquisition of vancomycin-resistance genes results in the rise of vancomycin-intermediate S. aureus (VISA). Herein in this study, we report the antimicrobial and anti-biofilm activity of cannabidiol (CBD) and CBD formulations containing minor cannabinoids against multidrug-resistant (MDR) MRSA and VISA strains harboring genetically defined resistance mechanisms.

METHODS

Isolation of non-psychoactive cannabinoids

The non-psychoactive cannabinoids were extracted from Cannabis sativa plants using commercial extraction methods. The CBD was further purified using distillation, extraction and crystallization techniques. The minor cannabinoids were further purified from crude extract using chromatographic techniques.



Characterization of cannabinoid compositions

The chemical composition of cannabinoids was quantified by using high performance liquid chromatography (HPLC) and UV spectrometry.

Minimal inhibitory concentration determination

The minimal inhibitory concentration (MIC; µg/ml) of pure CBD isolate as well as CBD formulations containing variable amounts of minor cannabinoids (CBC, CBN, CBDV and CBG) was determined using the broth microdilution method using S. aureus strains with genetically defined resistance mechanisms.

Biofilm formation assay

The effect of CBD alone and in combination with minor cannabinoids on S. aureus biofilms formation and development was characterized by using spectrophotometric crystal violet (CV) assay.

RESULTS

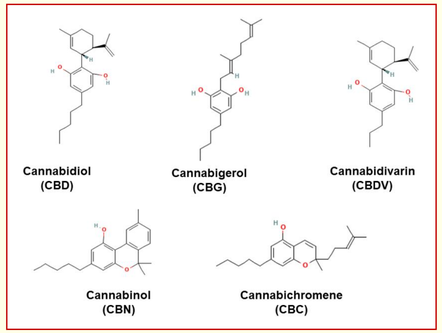

Figure 1. The chemical structures of major, non-psychoactive cannabinoids isolated from Cannabis sativa plant.

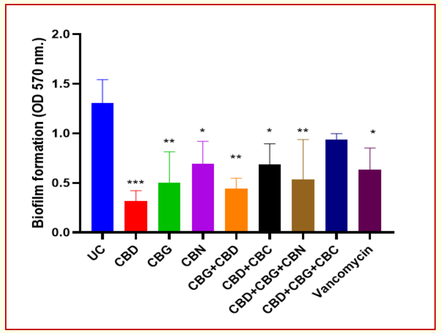

Figure 2. The effect of cannabinoids on S. aureus MRSA biofilm formation. The biofilms were exposed with 1X MIC concentration of test compounds for 24 hours.

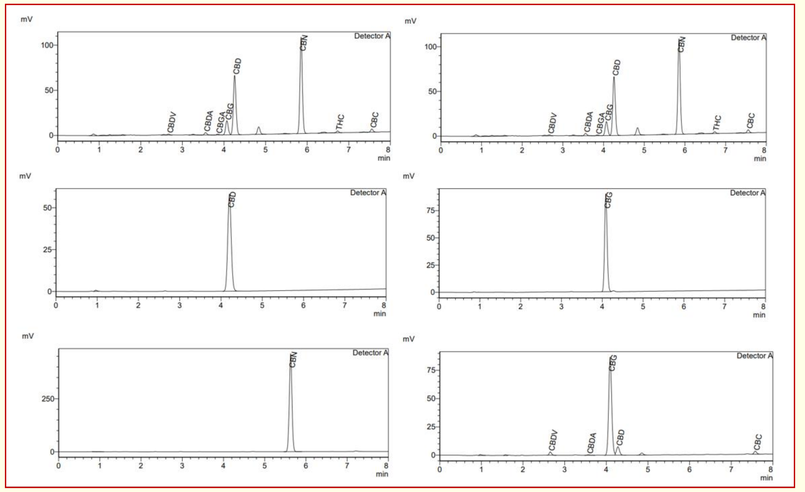

Figure 3. The detection and characterization of major cannabinoids extracted from C. sativa. The cannabinoids of interest were further purified by using liquid chromatography and their chemical purity was confirmed by HPLC.

Table 1. The minimal inhibitory concentration of non-psychoactive cannabinoids against Staphylococcus aureus isolates with genetically defined resistance mechanisms.

Pathogen	Resistance mechanisms	MIC							
		CBD	CBG	CBN	CBG+CBD	CBD+CBC	CBD+CBG+CBN	CBD+CBG+CBC	Vancomycin
S. aureus Pan-S	*blaZ*	1	1	2	8	32	64	8	0.5
S. aureus MRSA	*mecA*	2	4	2	16	16	64	8	2
S. aureus VISA	*aac(6')-aph(2'')*, *aadD*, *ermA*), *mecA*, *spc*, *tet(M)*	1	4	2	32	32	128	2	8

Pure CBD, CBG and CBN demonstrated satisfactory and selective antimicrobial activity (2-4 µg/ml) against all tested MRSA and VISA strains and was comparable or greater than vancomycin (1-2 µg/ml and 4 µg/ml, respectively).

CONCLUSIONS

These results demonstrated the promising translational application of CBD as a novel candidate for future development of novel antimicrobial candidates targeting multidrug-resistant Staphylococcus aureus and their biofilms.

REFERENCES

1. Blaskovich MAT, Kavanagh AM, Elliott AG, Zhang B, Ramu S, Amado M, Lowe GJ, Hinton AO, Pham DMT, Zuegg J, Beare N, Quach D, Sharp MD, Pogliano J, Rogers AP, Lyras D, Tan L, West NP, Crawford DW, Peterson ML, Callahan M, Thurn M. The antimicrobial potential of cannabidiol. Commun Biol. 2021 Jan 19;4(1):7. doi: 10.1038/s42003-020-01530-y. PMID: 33469147; PMCID: PMC7815910.
2. Martinenghi LD, Jønsson R, Lund T, Jenssen H. Isolation, Purification, and Antimicrobial Characterization of Cannabidiolic Acid and Cannabidiol from Cannabis sativa L. Biomolecules. 2020 Jun 12;10(6):900. doi: 10.3390/biom10060900. PMID: 32545687; PMCID: PMC7355595.

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