



Marijuana and Tuberculosis and Alteration of Th1/Th17 Responses: Advantage or Disadvantage or Neutral?

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Background: Medical marijuana is a new concept in using legalized cannabis for the management of medical disorders. At present, this new concept is used in many countries. Medical marijuana might be useful for the management of many disorders including tuberculosis. Here, the authors study on immune response alteration resulted from marijuana use for tuberculosis management. **Methods:** The standard bioinformatics clinical pathway analysis is performed to access the interrelationship between pharmacotoxicological process of active ingredients of marijuana and pathophysiological process of tuberculosis with T-helper (Th) 1/Th7 response as a linkage node. **Results:** From the interrelationship study, there is a coacting phenomenon that can promote infection. **Conclusions:** Marijuana can impair Th1/Th7 response. Marijuana is not benefit for tuberculosis management.

Key words: Marijuana, response, T-helper cell, tuberculosis

INTRODUCTION

Marijuana or cannabis is an important plant that has been found in tropical areas. This is a well-known plant due to its various health effects. Marijuana can cause many adverse effects inducing addiction and psychological reaction. Therefore, marijuana is categorized into narcotic plant groups. Due to possible pharmacological advantage, legalization of marijuana for medical use is implemented in many countries worldwide.^{1,2}

Medical marijuana is a new concept in using legalized marijuana under controlled by medical specialist for the management of medical disorders. The rational for utilizing medical marijuana is making use of the pharmacological advantage of marijuana under strict legal control.³ There are many advantages of medical marijuana for the management of many disorders such as pain syndrome and neurological problem.^{4,5} Medical marijuana is claimed for the advantage in the management of several infections including tuberculosis.^{6,7} The advantage of marijuana is due to its important active chemical components, $\Delta(9)$ -tetrahydrocannabinols (THC).⁷ THC are psychoactive substances with poor water solubility found in marijuana.⁸ Pharmacologically, THC act through

cannabinoid receptor 1 in the central nervous system. This action results in euphoric emotional change relief of stress and pain reduction.⁸ At present, medical marijuana are applied in many diseases such as Parkinsonism and malignancy.⁸ THC have several actions after the administration into the human body.⁹ THC play a role that can induce positive affective and reinforcing effects. Nevertheless, the repeated exposure to THC results in dependence or addiction.^{9,10} THC can also induce immunomodulation through cytokine pathway adjustment.¹¹ The specific immunopharmacology and immunopathology of this biological process are very interesting. Here, the authors study on T-helper (Th) 1/Th7 response alteration due to marijuana use for tuberculosis management.

METHODS

This work is a clinical bioinformatics study by pathway analysis. The aim of this study is to access the interrelationship between pharmacotoxicological process of active ingredients of marijuana and pathophysiological process of tuberculosis, with

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immune response as a linkage node. The protocol for the present study is directly quoted from the previous publication.¹² First, the authors performed a literature searching using databases, PubMed and SCOPUS for identifying published article regarding the immune response process relating to THC and tuberculosis. The specific search keywords were “immune,” “tuberculosis,” and “marijuana.” The reports with details on pathways were recruited for further common interrelation linkage identification. The linkage node was identified, and then, the final interrelation mapping to represent final common pathway diagram was performed. This work is a pure clinical bioinformatics study and does not deal with animal or human cases; therefore, informed consent or ethical approval is not applicable.

RESULTS

From the interrelationship study, there is a coacting phenomenon through Th1/Th17 immune response linkage.¹²⁻¹⁴ This phenomenon results in promoting tuberculosis infection. The rearranged common pathway is presented in Figure 1. The marijuana does not suppress, but it promotes tuberculosis infection.

DISCUSSION

The use of the active gradients from medicinal plants for the management of medical disorder is interesting. To find for new

drugs, medical scientist usually seeks for new active chemicals from the several plants. Medical marijuana is an interesting present concept. After legalization, there are many studies on the medical advantages of marijuana. Similar to many ethnomedicinal plants, the advantage of marijuana is not well demonstrated. The two important primary active components of marijuana include Δ^9 -THC and cannabidiol.⁴ Marijuana plays pharmacological action through endocannabinoid system. This action is useful for the management of many medical problems such as pain, memory impairment, nausea, and vomiting.⁴ Both cannabidiol Δ^9 -THC and spasm can help decrease pain, but Δ^9 -THC also induces unwanted psychological effects.⁴

The antibacterial property of marijuana might be useful for infectious disease management.¹⁵ The interrelationship between marijuana and lung disease is still inconclusive.¹⁶ Some researchers report that marijuana has a bad effect on the lung while the others report on opposite findings.¹⁶ There is a report that cannabidiol can induce degradation of *Mycobacterium spp.*¹⁷ The use of medical marijuana for the management of tuberculosis is very interesting.

Despite there are limited modern scientific proofs, marijuana has been used by some local ethnic minorities as local wisdoms for the management of respiratory disease for a long time.¹⁸ The good example is the use of marijuana for the management of lung disease including tuberculosis in the Thai traditional medicine regimen.¹⁹ It is interesting and rational to perform a study to proof on the exact usefulness of marijuana for the management of the disease. Bioinformatics is a preliminary safe technique that can give primary data for further *in vivo* and *in vitro* studies. In the present report, the authors used standard pharmacoinformatics technique for clarification whether the medical marijuana should be useful for tuberculosis treatment or not. How marijuana modifies pathophysiology of pulmonary tuberculosis is still not well understood. The present work is a preliminary study to clarify this specific issue. Focusing on immunological alteration by medical marijuana, THC can suppress the Th1/Th17 response. The suppression process results from the action of Δ^9 -THC on cannabinoid receptors expressing on immune cells. THC can deactivate lymphocytes and Th1/Th17 lineages biological pathway, which further results in immune suppression.¹³ The Δ^9 -THC can suppress Th1 production of interferon gamma by decreasing the levels of mRNA encoding for Th1-related cytokines²⁰ and can inhibit Th17 activation through similar regulation of mRNA encoding for Th17-related cytokines interleukin-17 (IL-17), IL-21, IL-22, and IL-23.¹³

The described effects of marijuana can modify the immunopathophysiological process in tuberculosis. The immunodefense mechanism to tuberculosis is mainly

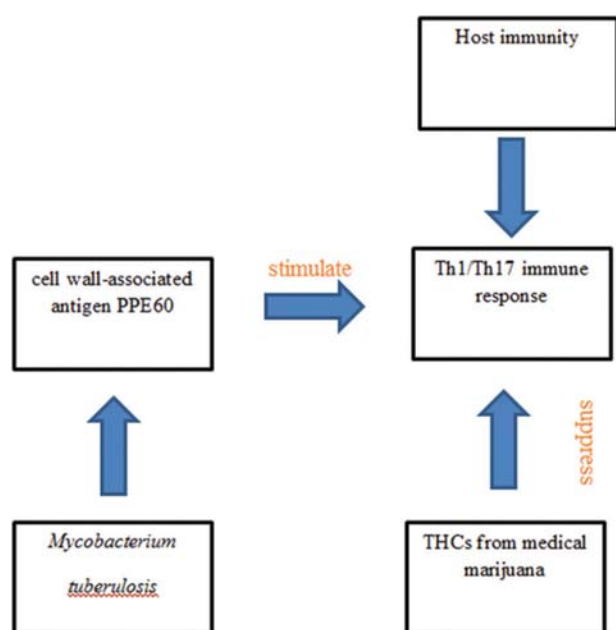


Figure 1: Pathway showing patho-biological interrelationship due to effect of tetrahydrocannabinols from medical marijuana and tuberculosis infection

through Th1 proliferation that can further result in surges of Th1-related cytokine.²¹ Th17 also play a similar role in defending tuberculosis through Th17-related cytokine.²² In tuberculosis infection, there is a direct Th1 and Th17 destroys by mycobacterial pathogen, which can result in the suppression of previously mentioned Th1- and Th7-related defense mechanisms.

Therefore, the marijuana-related immune suppression results in impaired defensive immunological mechanism to tuberculosis. In addition, there is impaired Th1/Th17 response due to pathogenic peptide from tuberculosis. Basically, an overproduction of Th17-related cytokines in tuberculosis patients is a basic physiological reaction to limit tuberculosis pathology.¹⁹ Pathologically, Th17-like T-cell subsets are dysregulated by pathogenic *Mycobacterium tuberculosis* and there will be the progression of tuberculosis if there is ineffective immunological function of the T-cells or T-cell exhaustion.²² Therefore, there is a superimposed Th1/Th17 suppression when medical marijuana is given to the tuberculosis patient. Step by step, the tuberculosis pathogen counteracts and destroys immunological defense mechanism of the patient. If there is an additional marijuana effect, there will be an additional suppression on cytokines produced by Th1 and Th17 cells that are left from destroy by tuberculosis pathogen. Therefore, marijuana is not benefiting but cause additional unwanted problem in the management of patient with tuberculosis.

Therefore, marijuana is not beneficial for tuberculosis management. On the other hand, it is problematic. In fact, marijuana can result in tuberculosis outbreak.^{23,24} Sharing same set of pipe living in the same ambient air in the same area of the group of marijuana users are the main causes of tuberculosis spreading.^{21,22} The immunity suppression is an unwanted consequence of medical marijuana. Since medical marijuana is also used for the management of patient with human immunodeficiency virus (HIV) infection, the increased impaired helper T-cell function might occur and further result in the increased incidence of tuberculosis among HIV-infected patients.

This study is a preliminary bioinformatics interrelationship study. There are some limitations of the study. From the interrelationship study, there is a coacting phenomenon through Th1/Th17 immune response linkage. Nevertheless, interaction among Th1/Th17/Treg is complicated. Further, studies for clarifying how marijuana influences the T-cells are suggested.

CONCLUSIONS

Based on the present study, marijuana can cause deterioration in Th1/Th7 response, and it is not be useful for the management of tuberculosis.

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Conflicts of interest

There are no conflicts of interest.

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