Indian researchers use a novel route to kill TB bacteria

A compound isolated from shala trees modulates the immune system to kill the bacteria

A team of Indian researchers has been able to achieve 100-fold reduction in TB bacterial load in lungs of mice after 60 days of treatment using bergenin — a phytochemical isolated from tender leaves of sakhua or shala tree (Shorea robusta). Unlike the regularly used antibiotic drugs that target the TB bacteria, the bergenin compound modulates the immune system to kill the bacteria found inside the macrophages (a type of white blood cells). The results were published in the journal Frontiers in Cellular and Infection Microbiology.

“Our studies show that the bergenin compound can be used to clear the bacteria, and when used in combination with other TB drugs can produce good results,” says Gobardhan Das from the Special Centre for Molecular Medicine at Jawaharlal Nehru University (JNU), a corresponding author of the paper. “Since the compound does not target the bacteria directly but modulates the immune system to kill the bacteria, it can be used in patients with drug-resistant TB too.”

The researchers undertook several studies to understand the mode of action of the compound. The compound was unable to directly kill TB bacteria when treated with the compound. However, in the case of in vitro studies, the compound was able to kill the bacteria found inside infected cells. In mice infected with TB and treated with the compound, there was significant reduction in the bacterial load in the lungs. Unlike in the case of in vitro studies, in mice the compound was found to activate not only the macrophages but also other cell types (T cells) that led to effective killing of the bacteria. A significant reduction in the number of granulomatic lesions was seen in animals treated with the compound. Also, the bacterial load was 100-fold lower in mice treated with the compound compared with controls (animals that were not treated with bergenin). “These findings strongly suggest that the immune response enhanced by the compound is able to increase the capacity to clear the TB bacteria,” Prof. Das says.

The levels of nitric oxide and a cytokine (TNF-alpha) were found to be enhanced. “We found the bergenin compound was selectively enhancing the frequency of interferon-gamma and interleukin-17-producing T cells in the TB infected animals,” says Dhiraj K. Singh from ICGEB and a co-author of the paper. Interferon-gamma promotes bacteria-killing nitric oxide inside macrophages thus promoting the generation of protective immune responses against TB bacteria.

Previous studies have shown that T helper 1 (Th1) cells play a key role in protecting the host against TB bacteria, while Th2 cells oppose the protection offered by Th1 cells. “There is a dynamic balance between the Th1 and Th2,” says Ved P. Dwivedi from ICGEB and the first author of the paper. “While TB bacteria prevents Th1 response and facilitates Th2 response, the bergenin compound promotes the expression of Th1 and Th17 responses.”

Beats conventional drugs

The compound has been shown to heal wounds faster than conventional drugs. Dr. Debprasad Chattopadhyay, Director of the ICMR-National Institute of Traditional Medicine (ICMR-NITM) in Belgaum, Karanataka, and the other corresponding author of the paper, had isolated the compound. He had seen tribals using the leaves of shala tree for wound-healing.

“Our study, in a limited way, tries to correct the misinformation regarding Ayurveda. The stage is now set to test many more Ayurvedic and plant-derived natural products for their potency against pathogenic diseases,” says Dr. Anand Ranganathan from the Special Centre for Molecular Medicine at JNU and one of the authors of the paper.

Prof. Das with the help of ICMR-NITM plans to carry out further tests in larger animals. If used in combination with other TB drugs the compound can shorten the duration of treatment and prevent the emergence of drug-resistance, the authors write.