

*Editorial***Tuberculosis and Traditional Medicine: Fighting the Oldest Infectious Disease Using the Oldest Source of Medicines**

Farzad Kobarfard

Tuberculosis (TB) is the oldest documented infectious disease. Fragments of the spinal column from Egyptian mummies from 2400 B.C. shows definite pathological signs of tubercular decay. The term phthisis (consumption) appears first in Greek literature. Hypocrates identified phthisis as the most widespread disease of the times around 460 B.C. Exact pathological and anatomical descriptions of the disease began to appear in the seventeenth century. In 1720, the English physician Benjamin Marten in his publication, "A New theory of consumption", mentioned that TB could be caused by wonderfully minute living creatures". The introduction of the sanatorium cure provided the first really step against TB. Hermann Brehmer a botany student suffering from TB, was instructed by his doctor to seek out a healthier climate. He traveled to the Himalayan mountains where he could pursue his botanical studies while trying to rid himself of the disease. He returned home cured and began to study medicine. In 1854, he presented his doctoral dissertation under the title, "Tuberculosis is a Curable Disease". This step became the blueprint for the development of sanatoria. In 1882, Robert Koch discovered a staining technique that enabled him to see *Mycobacterium tuberculosis*. By this means the deadliest enemy of humanity had been visualized and the war against this enemy was officially declared. The measures available to physicians were still modest. Improving social and sanitary condition and adequate nutrition were all that could be done to strengthen the body's defenses against the TB bacillus. Sanatoria provided a significant improvement. A further important development was provided by the French bacteriologists Calmette and Guerin, who used specific culture media to lower the virulence of the bovine TB bacterium, creating the basis for the BCG vaccine. Then in the middle of world war II came final break through, the greatest challenge to the bacterium that had threatened humanity for thousands of years: chemotherapy. Compounds such as sulfonamides and penicillins were ineffective against *Mycobacterium tuberculosis*. The first successful chemotherapeutic agent against *M. tuberculosis* was introduced to clinic by Selman A. Waksman and his team in 1944: streptomycin, purified from *streptomyces griseus*, showed a strong inhibitory effect on *M. tuberculosis* with relatively low toxicity. A succession of anti-TB drugs appeared in the following years: p-aminosalicylic acid (1949), isoniazid (1952), pyrazinamide (1954), Cycloserine (1955), ethambutol (1962) and rifampin (rifampicin in 1963) were introduced as anti-TB agents.

Introduction of these chemotherapeutic agents to the clinic resulted in a remarkable decline in TB cases all over the world. But it did not take a long time for *mycobacterium tuberculosis* to find its way around these compounds. Resistant species emerged in a short period of time and in order to tackle this problem Physicians started using different protocols of combination therapy. Since it is very unlikely that a single bacillus will spontaneously mutate to resistant to more than one drug, giving multiple effective drugs simultaneously will inhibit the multiplication of these resistant mutants. Therefore it was absolutely essential to treat TB patients with the recommended four drug regimens of isoniazid, rifampin, pyrazinamide and ethambutol or streptomycin. Having these powerful weapons in armamentarium, the battle against tuberculosis at least in industrialized countries seemed to be over during 70s. However, the emergence of multidrug resistant TB allowed *Mycobacterium tuberculosis* to escape the current drug arsenal and created frightening epidemics in affected

countries. In the absence of an effective therapy, patients with MDR TB continue to spread the disease, producing new infections with the resistant strains. Until new drugs which are effective against MDR strains are introduced, TB epidemic will grow at an exponential level. The other alarming fact is that the outbreak of HIV during the 80s has accelerated the spread of TB all over the world. Today TB is the leading cause of death worldwide from a single human pathogen. One third of the world's population is currently infected with *M. tuberculosis*; 10% of infected cases will develop clinical disease. According to the world Health Organization (WHO) facts sheets, TB kills 2 million people each year. It is estimated that between 2000 and 2020, nearly one billion people will be newly infected; in other word someone in the world is newly infected with TB every second. 200 million people will get sick and 35 million will die from TB if control is no further strengthened. The global resurgence of tuberculosis and development of drug resistance, call for urgent attention. No new class of anti-tuberculosis agents have been developed since the introduction of rifampin in to clinical in 60s. Thus there is a great need to search for and develop new anti-TB agents.

As it is obvious from the history of tuberculosis, man has been struggling with this disease for thousands of years and fighting against TB remains as a major challenge to all nations. Considering the long history and worldwide prevalence of TB, one could be certain that all different ethnic and cultural groups around the world have encountered this disease and used various methods and remedies in order to cure it through the past several centuries. Scientific study of the methods and materials used by these communities could lead to the discovery of new potential anti-TB drugs. For as long as man can remember, plants have been used worldwide in traditional medicines for the treatment of different diseases. The large diversity of plants in the world makes the technique of random screening a rather hit or miss process. It is quite obvious that using traditional medicine as a basis of selecting the starting point for new drug discovery results in a significant increase in the "hit rate" for the discovery of novel lead compounds compared with random screening. In the past this has led to the discovery of many important therapeutic agents; for example the antimalarial quinine from cinchona bark, the cardiac stimulant digitalis from foxgloves and the antidepressant reserpine isolated from *Rauwolfia serpentina*.

Another point which supports the ethnopharmacological approach to new drug discovery is the fact that a plant material has been used for several generations in a particular culture and it is likely that there would be no serious adverse effects associated with the regular use of the material. The active compounds isolated from natural sources are often highly complex in structure making them difficult to synthesize. This could be accounted as a disadvantage at the first sight, but it should be mentioned that if it had been left to synthetic organic chemists, they would have never attempted to make compounds with the complexity of natural products such as taxol or artemisinin. With the urgent need for new anti-TB agents, it is particularly appropriate to launch a comprehensive anti-TB screening program based on data collected from traditional medicine. Traditional medicine may be highly secretive, mystical and extremely localized; therefore it is essential to refine the information obtained from traditional practices in each region. The most efficient individuals to perform this task are local scientists since they are familiar with the regional cultures and are capable of communicating with the local traditional health practitioners. Given the current status of TB around the world, it is clear that tuberculosis is a global threat. However in order to explore the potentials of traditional medicine in the fight against TB, local actions must be taken by local authorities and scientists in order to be successful in this global challenge.

*Farzad kobarfard is currently working as an assistant professor in medicinal chemistry department of Shaheed Beheshti School of Pharmacy. He is also head of Tuberculosis drug development sector in Shaheed Beheshti Pharmaceutical research center. E-mail: [farzadkf@yahoo.com](mailto:farzadkf@yahoo.com)*