Plant-based siderophore: a new avenue in molecular medicine for tuberculosis

Mycobacterium tuberculosis remains a serious threat to human health, despite significant research on this organism. Study of *M. tuberculosis* has received increased attention because of an increase in cases of tuberculosis worldwide and a rise in incidence of drug-resistant strains.

Advances in mycobacteriology such as the completion of the *M. tuberculosis* genome sequence and comparative genomics using microarrays have provided impetus to the gathering of knowledge regarding the pathogenesis of this bacterium (Cole *et al.*, 1998; Wilson *et al.*, 1999). Understanding the molecular pathophysiology of this organism has led to the development of novel therapeutic approaches. However, peptides, proteins and nucleotides or DNA fragments, the new generation of tools against this infection, are facing problems resulting from transport, large molecular dimensions, instability at physiological pH or sensitivity to temperature. Therefore, revealing the fundamental factors regarding the host–pathogen interaction is a prerequisite for the development of new drug regimens or alternative therapies for this disease.

Mammalian host defence against the pathogen involves restricting access of the organism to iron. *In vitro* growth studies using standard culture media indicate that siderophore-mediated iron acquisition plays a critical role in growth and metabolism of *M. tuberculosis* (Olayanmi *et al.*, 2000). Iron confers a distinct advantage on mycobacteria in their survival in the hostile host environment. In response

to iron starvation, mycobacteria produce siderophores, iron-storage protein or receptors. Currently, little is known regarding the uptake of iron by the mycobacterial siderophore and the importance of siderophores in mycobacterial pathogenesis. However, exochelins (siderophores) of *M. tuberculosis* are capable of removing iron from the transferrin lactoferrin and transferring it to the cell wall of mycobacteria (Gobin & Horwitz, 1996). A ten-gene cluster spanning 24 kb of the *M. tuberculosis* genome encoding enzymes for production of a siderophore (mycobactin) has been reported (Quadri *et al.*, 1998).

Recently, a compound has been isolated from a root extract of the leguminous plant *Tephrosia purpurea* that solubilizes the compound rock iron $[\text{Fe}(\text{OH})_3]$ and helps in plant metabolism (Aggarwal *et al.*, 1999). This compound is also capable of inhibiting growth of *M. tuberculosis* H₃₇RA under *in-vitro* conditions (Rajiv *et al.*, 2001). The mechanism of action of this compound is through competition with the bacteria for iron in the environment.

We therefore propose a search for plant-based compounds that will generate new avenues to be exploited for human protection against tuberculosis. The future challenges to be met include determining the value of such plant-based compounds against invading bacteria and their effects on different components in the eukaryotic cell. This will resolve the formulation of these compounds and define an appropriate delivery system for the treatment of this infection.

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