CSIR develops a low-cost method for production of antiretrovirals


Dr Moira Bode

The CSIR announced on World Aids Day, December 1, that it had successfully developed an economically-competitive route for the local production of a key ingredient in antiretrovirals.

The project was initiated in 2004. According to Dr Moira Bode, who led the research team, efforts were focused on reducing the costs of producing thymidine - an important intermediate used in the pharmaceutical preparation of anti-HIV drugs such as stavudine and AZT. It is also hoped that the research outcomes would stimulate the establishment of a local active pharmaceutical ingredient (API) manufacturing industry - currently absent in South Africa.

The CSIR achieved its primary goal by using biocatalysis as opposed to employing chemical reaction techniques. Biocatalysis involves the utilisation of natural catalysts such as enzymes to perform chemical transformations on organic compounds. Enzymatic reactions are typically used in the food and beverage industries but are also becoming increasingly popular in the pharmaceutical industry.

Bode said the interdisciplinary team of molecular biologists, biochemists, chemists and process chemists investigated a process that works based on enzymes isolated from a bug not used before in this type of application in conjunction with another enzyme.

"Our research included total development of the biocatalysis reaction to produce 5-methyluridine as well as the chemistry to convert 5-methyluridine to thymidine," says Bode. "This involved, among other things, initial screening work to identify useful enzymes, the fermentations to produce enzymes and the process development for scale-up of the biocatalytic reaction, as well as the chemistry. The entire process was scaled at the CSIR to produce thymidine at kilogram scale," she explains.

A techno-economic model developed by the team and Arvir Technologies (Pty) Ltd, a new start-up biotech company, confirms that the project has resulted in a method where thymidine raw material could be produced at a price that is extremely competitive compared to current market prices for the same product. The model also provides a forecast for the cost of constructing a manufacturing plant of a certain size.

The CSIR has filed a patent on its technology, which has been licenced to Arvir.

While antiretroviral drugs have proven to prolong the quality of life for many HIV positive individuals they do not eliminate the virus. CSIR Biosciences is exploring other approaches to combating the virus.

The aptamer technology research group was formed in 2006 and has discovered an aptamer with the potential to inhibit entry of HIV-1 — the prevalent strain in sub-Saharan Africa. This specific aptamer interferes with the binding of the viral protein gp120 to host cell natural receptors. GP120 is the conduit through which HIV/Aids is able to attach itself to the human cell wall and gain entry into its host. Aptamers are small RNA-based nucleic acid molecules that have been found to display antiviral activity, among other characteristics.

The plant biotechnology research group in collaboration with several research partners investigated the expression of an HIV-1 antigen in plants. Plants offer a cost-effective alternative for the production of health molecules. The team's research is being further investigated for potential use as a sub-unit vaccine.

The bioprospecting group led by Dr Vinesh Maharaj is tapping into indigenous knowledge systems and employing scientific validation mechanisms to validate potential leads for treatment of HIV/Aids.