

## Affordable Malaria Treatment: Hope for Millions

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## Public-Private Partnership Excellence Award 2011

Utilizing public and private funding, Jamia Hamdard and Ipca Laboratories are engaged in a project to enhance the artemisinin content in *Artemisia annua L* plants. This is a big step towards making malaria treatment affordable and accessible in the South East Asian and African countries, where this disease is an endemic

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According to the World Health Organization (WHO) recommendations issued in April 2006, the treatment of uncomplicated malaria with artemisinin-based combination therapies (ACTs) can protect the artemisinins and the partner drug from resistance in the wake of reduced efficacy of the well-known once-first-line antimalarials such as chloroquine, and sulphadoxine-pyrimethamine. However, due to short supply of artemisinin, the cost-per-treatment course of ACT (108.70) over conventional antimalarial drugs (4.60) is high.

Consequently, the prices of these drugs are subsidized with government funds or with funds obtained from charitable organizations. Therefore, to meet the global demand of artemisinin, it is required that the plant *Artemisia annua L* (*A annua L*) should yield high amount of artemisinin uniformly throughout the population which has not been possible because of cross-pollination and variable segregation of segregants.

### Inception

Besides antimalarial property of *A annua L* plant, it has shown great potential in treating some other infectious diseases like schistosomiasis, HIV, hepatitis-B, leishmaniasis and a variety of cancer cell lines including breast cancer, human leukemia, colon cancer, and small cell lung carcinomas. This project will help to increase the income of farmers, thus stimulating their interest in the cultivation of *A annua L* plant. As the Indian economy is mainly based on agriculture, this project would help to strengthen the economy."

**Dr M Z Abdin** or type unknown

professor of biotechnology and dean, faculty of science, Jamia Hamdard University

Way back in 1994 when Dr M Z Abdin, professor of biotechnology at Jamia Hamdard University, started his research on *Artemisia annua* plants, he did not have the slightest idea that his research would get transformed into something gigantic after a decade. Dr Abdin who is now the dean, faculty of science, Jamia Hamdard, is confident about the high medicinal value of plants in curing malaria. Over a period of time, he continued with his research and strived to create better varieties of plants having better yield of artemisinin, which is required for the treatment. The funding agencies were reluctant to fund his initiative at first. However, Dr Abdin, supported by the university, relentlessly continued his efforts without losing focus. In 1994, the Department of Biotechnology (DBT), Government of India, provided funding close to 35 lakh for a project related to the study of biosynthetic pathway of artemisinin. After a gap of six years, he again got a funding of 10 lakh from the DBT for work on hmg co reductase enzyme and its regulation, which was actually related to the improvement of the plant variety. The research finally reached the stage

where ads gene from *Artemisia annua* was cloned and the regeneration protocol was optimized from the leaf explants. The whole plant was regenerated from the leaf explant and the transformation protocol was optimized using agrobacterium and binary vectors.

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"This project was in sync with the basic needs of the country's population and therefore it has been a huge step forward towards addressing the affordability issues in malarial treatment. Such partnerships must be encouraged and government agencies have to be more generous in their funding for those researchers who are working in key areas."

**Dr G N Qazi**

vice chancellor, Jamia Hamdard University

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Labs, converted into a new antimalarial drug Arteether and a new *Artemisia annua* variety for commercialization in India. This work was recognized with the CSIR Process Technology Award 1998, and the new plant variety 'Jeevan Raksha' was dedicated to the nation by the then Prime Minister of India, Atal Bihari Vajpayee, in 1999.

### Turning Point

The initial idea of Dr Abdin transformed into reality when in 2003 he met Dr D C Jain, while attending an international conference on malaria in New Delhi. After initial discussions, both realized that by working together, they could develop a new strain altogether. Around the same time, Dr Jain joined Ipca Labs Ratlam and collaborated with Jamia Hamdard for sharing information and work on a regular basis.

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"This project shows that prioritization of research in major disease areas can certainly make a big difference. I hope that we will be able to commercialize the product as soon as possible. India requires more of such initiatives for the larger benefit of the masses"

**Dr D C Jain**

general manager, Green Tech Department, Ipca Labs

engineering. Therefore, Ipca Labs signed an MoU with Jamia Hamdard in 2007 to collaborate in enhancing the yield of artemisinin by applying metabolic engineering approach.

Artemisinin is commercially produced from *Artemisia annua* L plants with a content of 0.01-1.0 percent. The Jamia research team, with the help of Ipca Labs, developed a novel strain of *A annua* L through bioengineering mevalonate and artemisinin biosynthetic pathways by over-expressing hmgr and ads genes, encoding key enzymes of these pathways. The bioengineered strain of *A annua* L had around 160 percent higher leaf biomass and 90.91 percent artemisinin as compared to the mother variety (received from Ipca Labs). More recently, Ipca Labs and the Department of Science and Technology (DST), Ministry of Science and Technology, Government of India jointly sponsored a major research project of Jamia Hamdard for developing a noble strain of *A annua* L with high artemisinin content through genetic manipulation in 2011.

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"When Ipca started out with this project, our objective was to increase the yield of the artemisinin content in *Artemisia annua* L plants which will be a great boon in the cure of malaria. This product is relevant to the population in countries like India and Africa where the incidence of malaria is high and anti-malaria drug is expensive. This product will ultimately be for the masses, because the project not only looks at scaling up production, but also looks at increasing availability and providing it at affordable prices to the population. Currently, it is in its lab stages and around 50-60 percent of the project is already complete at Jamia Hamdard"

**Dr Ashok Kumar**

economist of the country.â€

Echoing similar views, Dr D C Jain, says, "To carry out major research projects like the present one, the funds received from the government and the industry are extremely essential. They are used to hire manpower, chemicals, consumables and instruments. These components are important for the successful completion of the project."

### Scaling up efforts

At present, the stability and inheritance of trans hmgr and ads genes in the newly developed strain of *A annua* L plants is being studied. Also, the parameters related to growth and yield of artemisinin in this variety are being evaluated. It is being

While Dr Abdin was working in New Delhi, another scientist, Dr D C Jain, was also pursuing similar research in the area of antimalarial drug development from *Artemisia annua* at the Central Institute of Medicinal and Aromatic Plants (CIMAP), Lucknow. During the 90s, Dr Jain was the pivotal scientist in the successful implementation of the project at CIMAP. The efforts of Dr Jain, who now is the general manager, Green Tech Department, Ipca

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The biotechnology department of Jamia Hamdard had already conducted research to improve the yield of artemisinin by applying various approaches like agrotechnology and tissue culture. It had already engaged in developing transgenic lines of some important medicinal plants. But now was the time to use the other high-end technologies, such as genetic

engineering. Therefore, Ipca Labs signed an MoU with Jamia Hamdard in 2007 to collaborate in enhancing

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Jamia Hamdard has so far received 97.64 lakh from these agencies as funds for the project. While the role of Jamia has been to improve the varieties and develop new strain, Ipca Labs is focused on scaling up the production and commercialization of the product. Ipca Labs has funded 30 percent of the total cost of the project. According to Dr M Z Abdin, "The government agencies and the biotech industry should make efforts to run projects on the PPP model. This will facilitate major projects leading to the development of products, which ultimately benefit the public at large and support the growth of the biotech industry. It will also help increase the knowledge base and the

expected that the metabolic engineering approach pursued in this study will lead to the development of a novel variety of the plant with artemisinin content more than 1.5 percent. This variety can be patented and released to the farmers for mass scale cultivation and will ultimately lead to higher production of artemisinin.

After the Institutional Biosafety Committee at Jamia cleared the proposal, the application was filed before the Review Committee on Genetic Manipulation (RCGM) for the approval of confined trials of the genetically engineered plant followed by open field trials. After the clearance, Ipca Labs is expected to carry out field trials of this strain in 2012-13 seasons.

“Hopefully, the newly developed transgenic line of *A. annua* L plant will be commercialized by the end of 2014 and it would help to accommodate the gap between demand and production of artemisinin,” says Dr Abdin.

Ruling out fears that may arise due to the GM origin of the product, Dr Jain says, “Much hype has been created about GM crops, so it will be a little hard to make people accept such products. However, this product is very safe to use and harmless to people's health and environment.”

As per the conditions laid out at the time of the initiation of the partnership, the patent of the product will be owned jointly by Jamia Hamdard and the DST. At the same time, Ipca Labs because of its contribution, will get the first priority for using it commercially. While the revenue generated by the sale of the patent will be shared by Jamia and the DST, Ipca Labs would benefit at the commercial level with some percentage of earnings given to Jamia.

-Rahul Koul in New Delhi