

## "Traditional knowledge can benefit drug development�

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Natural products can be a tremendous primary source for modern drug discovery. However, the isolation and purification of the target product from plants represents one of most challenging tasks, which require the knowledge both at the molecular level and at the process level. On the one hand, there might be hundreds of compounds extracts from plants together with the target product: on the other hand, many of the compounds contained in the crude extracts may have similar chemical structures as the target compound. Therefore, it is a quite complex and challenging task to develop and synthesize the production process to produce the final target compound from the raw materials. One needs to identify the necessary unit operations and interconnect and integrate them in a systematic way to synthesize the whole production process. At the time, one needs to optimize the production process at both the unit level for the unit operations and the system level for the Whole process system to pursue the multi-objective optimized solution. The proposed synthesis method was applied to the design and development of the separation process for the isolation and purification of artemisinin which is the most effective antimalarial drug from the medicinal herb Artemisia annua.

Artemisia annua L. is native to China and commonly known as sweet wormwood and qinghao. Artemisinin is an antimalarial natural product principally obtained from the leaves of this plant. Artemisinin based ACTs are recommended by WHO for the treatment of complicated malaria; therefore, the world demand of this wonder natural product is increasing every year. Artemisinin is chemically a sequiterpene lactone with an endo-peroxide group. This endo-peroxide is responsible for its therapeutic group activity.

As artemisinin content in the plant was very low and variable and, therefore, its commercial production was a long cherished desire for scientists.Resaerchers have tried to establish its laboratory synthesis but due to tedious multiple step synthesis this

molecule remained a difficult challenge to synthetic chemists around the world.

Therefore, feasible commercial natural production is yet to achieve. While synthetic chemists were searching for the costeffective paths of its synthesis. Scientists were also working on enhancement of Artemisinin content through techniques of plant breeding coupled with biotechnology. Finally content of Artemisinin was achieved in the range 0.8 to 1.2 % w/w in commercial crops. Ipca has started commercial production in India from 2006.Ipca requirement for Artemisinin 40-50 MT per year for antimalarial drug production but we are fully dependent from outside sourcing.

Ipca has produced 2000 MT of Artemisia leaves in 2012-2013 and will target to achieve 3000-3500 MT in 2013-2014. Weare producing natural artemisinin and imparting employment in rural peoples of India, and reduced dependency to outside world.

Global cost of Artemisinin is variable and fall down in the below cultivation cost, some where affects its commercial agricultural extension but to beat these price fluctuations we have changed and strengthen our production system by incorporation of various latest technologies of extraction & purification. A higher, more consistent, improved process for higher yield of API and therefore low raw material consumption - would aid in stabilizing the volatile artemisinin market. Recently, a pharmaceutical company is establishing semi synthetic Artemisinin and the expected to start its commercial production by 2013.Artemisia is cash crop on top of food production it is the crop that keeps them out of poverty. The semi synthetic drug does exactly the opposite.

Interesting point is that some eminent persons are debating on price issues and ceasing of rural employment as affect by semi synthetic. A waste product (artemisinic acid) from Artemisia processing can be photochemically covert into artemisinin. This approach save the farmers through cultivation as well as supply the artemisinin. For Artemisinin we want to assure that commercial production of natural artemisinin is able to compete with semi synthetic artemisinin.

It would be important for the supply for the natural version of artemisinin to continue along side the semisynthetic production. We hope that the message will not be that it will replace the natural product, because this would acts as disincentive to the farmers, who could stop production their crops. It should be complementary with a growing share of the market. If complete replacement, greatly impact the sustainable use of biodiversity and fair and equitable sharing of benefits from the genetic resources that produce natural products.

Now the time comes to use our traditional knowledge for use for new drug development. The major reason not to convert traditional knowledge into viable drug against synthetic drug. The active molecule quantity is very small and recovery from plant material is not cost effective. Now using biotechnological approach to improve the plant varieties according to our active molecule requirement. The calibration improved the quality consistency of raw material. The material requirement for large scale production also fulfill by only sustainable cultivation rather digging from forest.

Recently new extraction and purification technology are available to achieve single or mixture of active compound with great purity. This can be standardized by modern techniques like HPLC, HPTLC, GC, GC- Mass etc natural products need scientific approach to deliver the components in a sustained manner to increase patient compliance and avoid repeated admistration. This can be achieved by designing novel drug delivery systems (NDDS) for herbal constituents.NNDSs not only reduce repeated administration to overcome non-compliance, but also help to increase the therapeutic value by reducing toxicity and increasing the bioavailability. One such novel approach is nanotechnology. Nano-sized drug delivery systems fo herbal drugs have a potential future for enhancing the activity and overcoming problems associated with plant medicines. Hence, integration of the nano carriers as a NNDS in the traditional medicine system is essential to conflict more chronic diseases like asthma, diabetes, cancer, and others.