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A Greener Approach towards the Synthesis of an Antimalarial Drug Lumefantrine

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Abstract : Malaria is a disease that kills approximately one million people annually. Children and pregnant women in sub-Saharan Africa lost their lives due to malaria. Malaria continues to be one of the major causes of death, especially in poor countries in Africa. Decrease the burden of malaria and save lives is very essential. There is a major concern about malaria parasites being able to develop resistance towards antimalarial drugs. People are still dying due to lack of medicine affordability in less well-off countries in the world. If more people could receive treatment by reducing the cost of drugs, the number of deaths in Africa could be massively reduced. There is a shortage of pharmaceutical manufacturing capability within many of the countries in Africa. However one has to question how Africa would actually manufacture drugs, active pharmaceutical ingredients or medicines developed within these research programs. It is quite likely that such manufacturing would be outsourced overseas, hence increasing the cost of production and potentially limiting the full benefit of the original research. As a result the last few years has seen major interest in developing more effective and cheaper technology for manufacturing generic pharmaceutical products. Micro-reactor technology (MRT) is an emerging technique that enables those working in research and development to rapidly screen reactions utilizing continuous flow, leading to the identification of reaction conditions that are suitable for usage at a production level. This emerging technique will be used to develop antimalarial drugs. It is this system flexibility that has the potential to reduce both the time was taken and risk associated with transferring reaction methodology from research to production. Using an approach referred to as scale-out or numbering up, a reaction is first optimized within the laboratory using a single micro-reactor, and in order to increase production volume, the number of reactors employed is simply increased. The overall aim of this research project is to develop and optimize synthetic process of antimalarial drugs in the continuous processing. This will provide a step change in pharmaceutical manufacturing technology that will increase the availability and affordability of antimalarial drugs on a worldwide scale, with a particular emphasis on Africa in the first instance. The research will determine the best chemistry and technology to define the lowest cost manufacturing route to pharmaceutical products. We are currently developing a method to synthesize Lumefantrine in continuous flow using batch process as bench mark. Lumefantrine is a dichlorobenzylidine derivative effective for the treatment of various types of malaria. Lumefantrine is an antimalarial drug used with artemether for the treatment of uncomplicated malaria. The results obtained when synthesizing Lumefantrine in a batch process are transferred into a continuous flow process in order to develop an even better and reproducible process. Therefore, development of an appropriate synthetic route for Lumefantrine is significant in pharmaceutical industry. Consequently, if better (and cheaper) manufacturing routes to antimalarial drugs could be developed and implemented where needed, it is far more likely to enable antimalarial drugs to be available to those in need.

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