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A study towards the synthesis of a hybrid bioartificial liver

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ABSTRACT

If one were to imagine the body as a chemical processing plant, then the liver would be equated to the reactor responsible for almost all the metabolic activities of the body. There is hardly any chemical produced, secreted or regulated that the liver is not directly or indirectly responsible for, making the design of an artificial liver a daunting task for any researcher. It is currently impossible to replicate the multitude of functions of a single liver cell, even given all the knowledge and technological advances of the 21st century.

An artificial liver should be able to supplement the failing functions, especially those of a detoxification nature, of an injured or diseased liver. This can be achieved by harnessing the natural capabilities of transformed hepatocytes for use in a hybrid artificial liver. Today, even with all the research currently taking place, liver transplantation is still the most common response to acute or chronic liver failure. The aim of this study was to develop a feasible theoretical design for a hybrid artificial liver reactor. This study draws on various disciplines such as biochemistry, medicine and engineering. A high-level systems approach was employed to the Process Synthesis. Process Synthesis methodology ensures efficiency in the design process which is achieved by conducting the laboratory experiments in parallel with the reactor or process design such that only those experiments or parameters that require optimisation need to be performed.

The capability of the selected transformed hepatocyte cell lines, HuH7 and HepG2 for specific liver functions; the intrinsic cells kinetics for the two cell lines and the sensitivity of the reactor design to the cell line incorporated were determined. The three liver function tests selected were: ammonia metabolism, lignocaine uptake and ^{99m}Tc-DISIDA uptake. Our laboratory data demonstrate that for all three functions, both the cell lines exhibit liver functionality and that their kinetics are fairly similar. This finding suggests that the type of cell line incorporated in the reactor does not appear to significantly impact on the reactor design. Hence, it would appear from the preliminary screening tests that the choice of cell line incorporated is not a key parameter. Since Chang's method of immuno-isolation by microencapsulation was employed, the kinetics of external mass transfer was compared to the intrinsic cell kinetics to determine the rate-limiting step. Results indicate that the capsular membrane does not significantly impede mass transfer and that intrinsic cell kinetics is the rate-limiting step. The research has demonstrated that a packed bed configuration is a feasible reactor type capable of including the

number of cells neccesary to effect the reaction rate essential for the adequate removal of substances required for artificial liver support.