

Improving lives through a bioartificial liver support system

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INTRODUCTION

Acute hepatic failure (AHF) or liver failure is a condition where liver function is rapidly lost over days to weeks. The mortality associated with this condition remains at 80-90% despite advances in ICU care. Viral hepatitis, drug and toxin-overdose are the most common causes of AHF. Treatment of AHF relies on supportive therapy (ICU care). Liver transplantation is the accepted current gold standard although the following problems are frequently encountered:

- Availability of donor organs
- Long term use of immunosuppressive therapy is required following transplantation
- Unnecessary transplantations may be performed where liver function would have recovered if the liver could have been supported
- High costs of the procedure.

Survival of AHF patients may be improved if an effective extra-corporeal liver support system was available and the need for liver transplantation reduced due to known capacity of the liver for spontaneous regeneration following recovery from AHF.

The aim of this project is to develop technology towards a novel bioartificial liver support system (BALSS) (Figure 1) that is capable of providing liver functions, in patients with acute liver failure, while housed outside the body (extra corporeal). This novel system was co-developed by the University of Pretoria and the CSIR and is now proprietary.

Novel aspects of this technology include:

- The introduction of an artificial perfluorocarbon (PFC) oxygen carrier in the BALSS (internationally patented)
- A 3D porous polyurethane scaffold housed in a radial flow bioreactor
- A unique cell harvesting method
- Comprehensive understanding of the technology due to extensive modelling
- Real-time monitoring and control of the BALSS.

The potential benefit of a BALSS in terms of improvement of quality and quantity of life for people with acute liver failure in SA (and internationally) remains huge. Additionally, the creation of an international vehicle for commercialisation, manufacturing, sales etc. would contribute directly to economic growth in SA through the earning of foreign exchange. Depending on the commercialisation model, job creation is also a potential outcome of the technology. However, significant milestones still need to be achieved to make the BALSS more lucrative to potential investors for commercialisation.

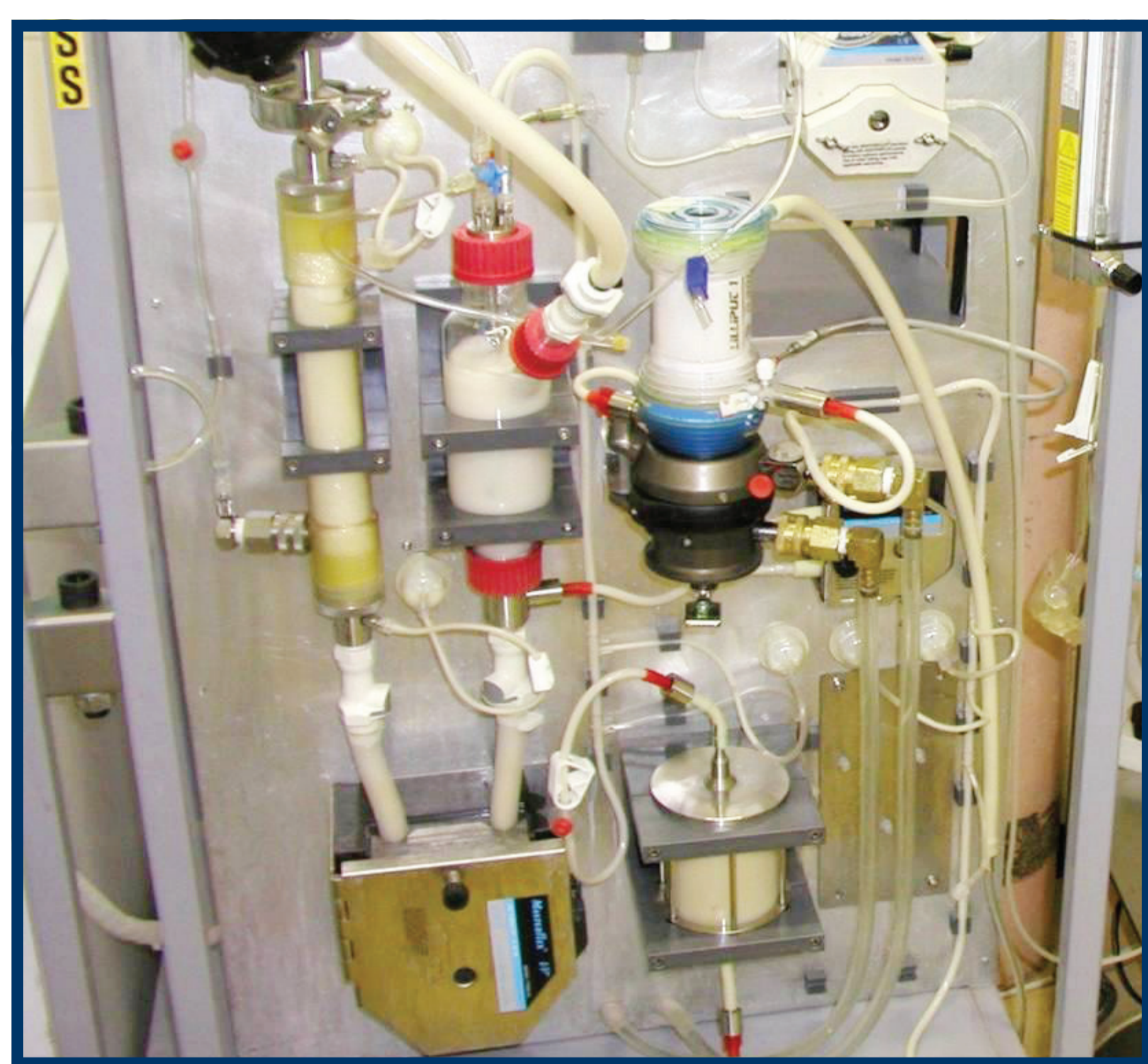


Figure 1: BALSS

SYSTEM DESCRIPTION

The BALSS treatment can be broadly compared to renal (kidney) dialysis treatment for patients suffering from kidney failure. The BALSS that we have developed is perfused with plasma obtained when cells are separated from the patient's blood. The BALSS device supports and performs the liver's essential functions such as synthesis of molecules, metabolic activities, detoxification and excretion before introducing the plasma back into the treated patient's body.

The BALSS consists of a bioreactor housing living primary hepatocyte (liver) cells attached to a three dimensional scaffold. Once the bioreactor is connected to the perfusion system, blood plasma from the patient is pumped (perfused) through the bioreactor. The hepatocyte cells in the bioreactor are sustained in optimal conditions by the introduction of an artificial oxygen carrier (perfluorocarbon or PFC) as well as by the close monitoring and control of the system parameters (Figure 2).

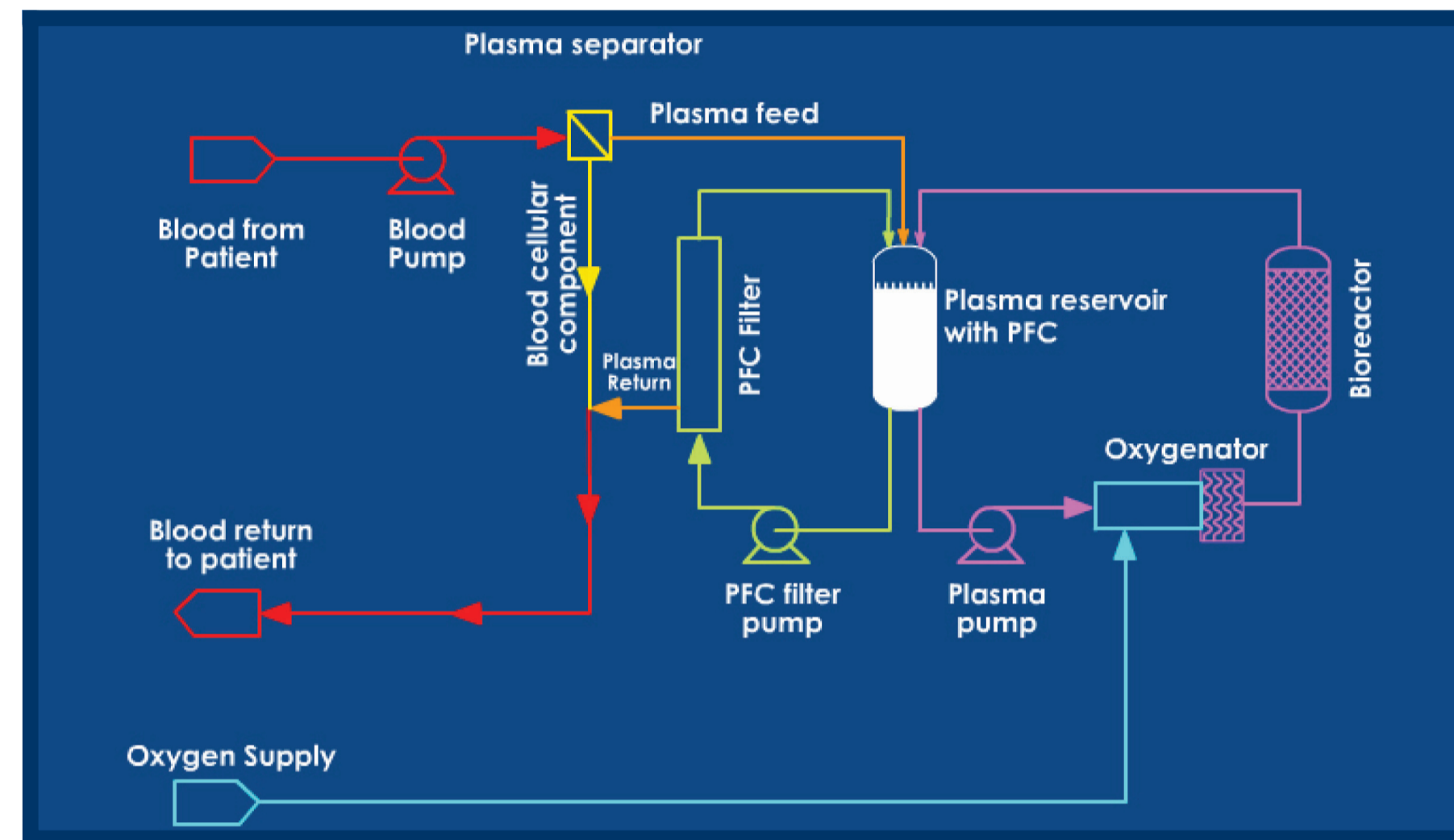


Figure 2: Schematic overview of BALSS circuit

Initial research and ex vivo cell experiments undertaken over the past financial years indicated the viability of the BALSS System. Extensive system analysis, design and material research led to the development of an animal test BALSS module, which underwent evaluation in *in vitro* and animal studies (Figure 3). Although the development of the BALSS has been completed successfully, substantial effort is still required in the development and commercialisation of the technology.



Figure 3: An animal trial conducted using the BALSS

MARKET POTENTIAL

The global market for BALSS technology is defined as patients suffering from acute liver failure or acute-on-chronic liver failure, and also those requiring treatment to prevent acute liver failure in progressive chronic liver disease. Typically, BALSS will address its defined markets through the following applications:

- Bridging patients with acute liver failure to transplantation
- Bridging patients with acute liver failure to recovery
- Bridging/support of patients with acute-on-chronic liver failure
- Post liver transplantation support
- Support/treatment of patients with chronic liver disease
- Support of patients with chronic/acute liver failure who do not qualify for transplantation
- Support of patients with partial liver transplants (e.g. living donor transplants).

Arbios Systems, a USA-based BALSS company, estimate the potential global market (2007) to exceed a massive USD 33 billion (Table 1). The USA and European markets are estimated to be almost USD10 billion with Asian markets expected to be more than double that at USD23 billion.

Table 1: Summary of potential target market (2007) [Reference: Arbios Systems Informational Brochure]

Number of cases per year	USA market or European market	Asian market	Global market (all countries)
Acute liver failure	10 000 liver failure episodes USD 750 million	200 000 liver failure episodes USD 2 billion	USD 3 billion
Acute-on-chronic liver failure	500 000 liver failure episodes 40% eligible, extracorporeal therapy USD 3,8 billion	10+ million liver failure episodes Est. 40% eligible, extracorporeal therapy USD 11 billion	USD 15 billion
Prevention of acute liver failure	Est. 100 000+ chronic patients USD 5 billion (plus)	Est. 1+ million chronic patients USD 10 billion (plus)	USD 15 billion (plus)

CSIR researchers are leading the way in bioartificial liver research to extend the lives of patients suffering from acute liver failure.

CONCLUSION

The bioartificial liver support system is a life saving and life enhancing product. It is aimed at any person who is suffering from acute-on-chronic or acute liver failure. These patients with hepatic diseases must receive a liver transplant or endure prolonged hospitalisation with an associated high mortality rate. The product has the objective of effectively and efficiently supporting patients until their own livers regenerate or in the more critically-ill patients, until a transplantation donor becomes available. Further commercialisation of this technology is presently being undertaken and if successful, will be a world first.