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REVIEW ARTICLE **OPEN ACCESS**

Artificial Liver tissue engineering: Solution to liver damage

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ABSTRACT
Liver is a crucial organ for the smooth metabolism of the human body but its failure carries a highly critical risk from health point of view. Liver failure is linked with high morbidity and mortality in absence of transplantation. Substitution of failed liver or restoring of genetically damaged liver invites requirement of liver donors. Additionally, shortage of donors worldwide for transplanted liver resulted in approximately 50% mortality amongst patients awaiting transplants. Thus, artificial liver proves to be one of the most promising substituent treatments for liver failure. This review summarizes the shortcomings due to liver failure problems and possible treatment through advanced artificial liver tissue engineering to overcome such medical issues.
Keywords: *Liver failure, Liver tissue engineering. Artificial liver.*

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INTRODUCTION

The liver is a complex organ perform various important functions in synthesis, detoxification and regulation; its failure therefore form a life threatening condition.[1] Liver failure (LF) can either occur without previous liver disease (acute liver failure, ALF), usually caused either by intoxication (Amanita phalloides, acetaminophen, methyl endioxymethamphteamine) or as acute decomposition of chronic liver-related illness (acute-on-chronic liver failure, AoCLF). In both cases, its symptoms include icterus, hepatic encephalopathy and disablement of condensation status and may result in multi organ failure. Exceptionally, liver failure may also be activated by certain diseases (Budd-Chiari-syndrome, Morbus Wilson) or pregnancy.

The only long-term therapy in certain cases is orthopaedic liver transplantation, unless the liver is able to regenerate. Many patients, especially those who are not listed for high acute transplantation, may not survive until a appropriate donor organ is available, since donor organs are rare. In other cases, contraindications do not allow liver transplantation. For these indications, extracorporeal liver serve devices have been developed in order to either link the patient to transplantation or temporarily the failing organ until it is able to regenerate.

In the case of liver failure, water-soluble toxins (e.g., ammonia, mercaptans) and albumin-bound toxins (e.g., bilirubin, bile acids, aromatic amino acids, fatty acids) may increase and cause encephalopathy and disorder of other organs. Artificial liver support system are devices which eliminate toxins which are collected from the blood. Hence, they work as filtration and absorption devices. These systems also help in getting lipophilic albumin bound organic material for example, bilirubin medium chain fatty acid, bile acids, and cytokines.[2] Acute liver failure (ALF) is life threatening so, patient liver transplantation is successful treatment for ALF patients as its 5 years survival rate increased by 75%.[3] Altered and mordernized version of artificial is construct in pre-clinical experiment on large animals. This artificial liver is not used in clinical experiment. So, it creates an important gap between clinical and pre-clinical studies.[4-6]

LIVER TRANSPLANTATION

Liver transplantation is examine when the liver not work effectively (liver failure). Liver transplants take from 6 hours to 12 hours. Throughout the operation, surgeons will throw out your liver and can

interchange it with the donor liver. Due to the fact a transplant operation is a main process, surgeons will must situation a pair of tubes in your body. These tubes are very essential to help your body to achieve special ability in the course of the operation and for a couple of days afterward.
Many issues involved in liver transplantation:-
Two of the most common issues are:

Rejection

Immune approach works to damage foreign elements that attack your physique. The immune system, however, are not allowed to distinguish between your transplanted liver and undesirable attacker, corresponding to viruses and microorganism. Thus, your immune approach could try and knock and break your new liver. That is introduce to as a rejection episode. Of all liver-transplant patients about 70% have some chances of organ rejection prior to discharge.

Infection

On the grounds that anti-rejection medicinal drugs that repress your immune system that are needed to avoid the liver from being rejected, you are at high threat for infections. This difficulty reduces as time passes. No longer of all patients have issue with infections, and most of the infections will also be managed efficiently as they occur.

METHODS OF DEVELOPING ARTIFICIAL LIVER

An artificial liver is a synthetic protective device which is present outside the body for a man and woman who is suffering from liver failure or disease. The principle of an Artificial Liver is to function a protective devices and uses liver cells bought from animals. As the device contains each organic and produce a components, it's called a "bio synthetic liver". The growing occurrence of liver sickness coupled with a recurrent scarcity of donor organs for transplantation has stimulate the development of many substitute treatment plans for liver failure. One of the critical leading strategy, extracorporeal bio-artificial liver instruments (BAL), has been under development for over forty years to accelerate recovery from acute liver failure or furnish a bridge to transplantation. BAL device are most of the time combine isolated hepatocytes with membrane-based bioreactors via which a patient's plasma could also be permeated. Bioreactor designs aim to protect phone viability and function without approaching a nutrient and metabolite trade so as to be therapeutically effective. Whilst latest trials have provided useful event in the implementation of BAL help, results have now not unambiguous validated efficacy. A sufferer's blood circulates through this bio-artificial liver, the place a certain synthetic membrane detached it from the animal cells. The membrane block the immunologic rejection of the cells, however allow the cells to detoxify the blood within the equal manner as a typical liver. Disposable units can be employed for a sequence of temporary cures, as with kidney dialysis. Already, the bio-artificial liver has saved the life of a person who used to be a patient of liver failure after it was found that cancer had sealed his bile duct.
Bio synthetic liver have the following functions-

1. Cellular add-ons should be purified and every aspect in it must be naturally recognized.
2. The cell education should be certainly shown to no longer transmit any infectious illnesses of any sort.
3. The mobile factor must be manageable and energetic
4. The factitious factor must be wholly biocompatible and integrity of the fabric and parts must also be proven.
5. The gadget have to be equipped to introduce the therapeutic and regulatory molecules that a healthy liver supplies, and it has to additionally filter elements from the blood in the way a usual liver does.
6. It must be immunocompatible.
7. Blood should perfuse competently through process

TECHNOLOGIES FOR ARTIFICIAL LIVER DEVELOPMENT:-

Hemodialysis/hemofiltration hollow fibers:

Indispensable for the managed interaction of cells and circulating fluids. Biomaterials technology can also be a key to this field. Many gadgets are composed of a phone populace surrounding an arrangement of hollow fibers. The fibers themselves and the fabric surrounding the fibers and cell phone population ought to both be biocompatible.

Maintenance of Cell line (hepatocyte cell line):

Cells used for liver healing must be ready to survive and/or proliferate within the gadget, and that they have to additionally keep their distinctive liver perform. Moreover, the undertaking of the cells themselves should not introduce hazardous substances into the body. Cells can also be remoted from liver tissue through digesting the extracellular matrix and proliferating the cells in vitro. Then a telephone remedy can be used to induce the cells to end up immortal.

Extracorporeal Device Designs:
Continued innovation in material science and engineering has extensively led to the development of extracorporeal liver-assist gadgets (ELAD). Along with new discoveries in telephone sourcing and hepatocyte stabilization, BAL instruments tailored to be used with hepatocytes are becoming a truth. The accessories of extracorporeal contraptions include the cellular factor, membrane element, and configuration.

CELLULAR COMPONENTS OF ARTIFICIAL LIVER:-
1. Primary Hepatocytes
They are the cells remoted immediately from the liver and have precise capabilities. If hepatocytes are isolated from porcine, proteins produced could have immunogenic response and barrier with infection, animal dealing with, and hepatocyte harvest, isolation, and storage process.
2. Immortalized telephone traces
Remodeling human hepatocytes are genetically engineered to proliferate and cells enable the device to work for longer time than most important hepatocytes. If cultured from humans, it produces human proteins and cells are comfortably on hand though cells most of the time lose function in vivo. However it is doubtful whether or not wholly differentiated hepatic and metabolic performance is maintained, hindrance of spontaneous mutations or changes in gene expression throughout culture. Some mobile phone strains are hepatoblastoma cellphone strains (tumor derived), which pose a theoretical danger of sufferer seeding.

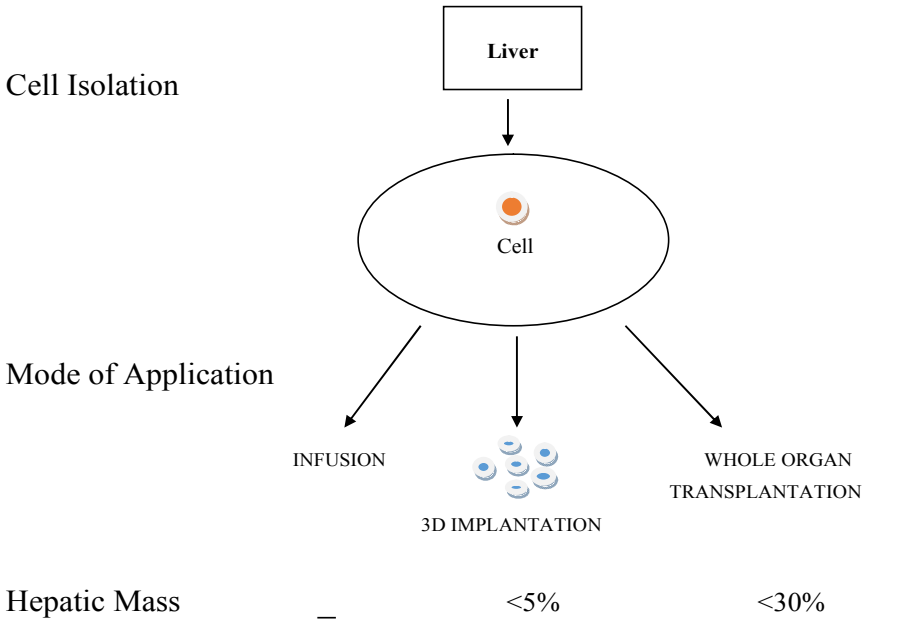

Figure1. Implantable Technologies For Liver Therapies

FUNCTIONS OF ARTIFICIAL LIVER:-
- Cellular components should be purified and every component in it must be clearly identified.
- The cellular preparation must be clearly shown to not transmit any infectious disease of any kind.
- The cellular component must stay viable and active.

- The device must be able to introduce the therapeutic and regulatory molecules that a healthy liver provides, and it must also filter substances from the blood the way that the normal liver does.
- Blood must perfuse properly through system.

ARTIFICIAL AND NATURAL SCAFFOLDS

Seeding cells into 3D scaffolds is one of the most exploited systems for the development of 3D platforms for in vitro culture. These scaffolds can be obtained from both synthetic and biological sources. Synthetic scaffolds can be easily engineered, but may also lack some key features, such as the physiological bioactivity and the biomechanics of the natural ECM. The most common artificial matrices used for engineering biological tissues are synthetic polymers (e.g., polylactide-co-glycolide, polyethylene glycol, and polycaprolactone)[7,8]and natural-derived hydrogels (e.g., alginates, celluloses, polyethylene).[9] 3D scaffolds can also be developed by using biological ECM-derived materials. For example, several substrates have been developed using basement membrane gels or type I collagen gels. However, the use of one or more ECM components does not summerize the biochemical and architectural complexity of a fully assembled natural ECM microenvironment and is in general specified by limited hepatocyte viability and function.[10]Therefore, functional substrates and scaffolds capable of providing a more appropriate microenvironment should be developed for the use of hepatocytes in liver tissue engineering, cell therapy, and transplantation.

To resolve these problems, attention has been directed to the development of biomaterials for functional tissue engineering by employing acellular tissues derived from the decellularization of tissues and organs. The process involves the complete removal of cellular material from the tissue while maintaining ECM protein composition, topography, and mechanical properties of the native tissue. Also the use of hydrogels reproducing the biochemistry of tissue-specific ECM proteins has been proposed. ECM hydrogels were obtained from decellularized rat livers and were used for both 2D-plate coating and *in vivo* hepatocyte transplantation. Primary rat hepatocytes which were cultured on a liver ECM hydrogel-coated substrate exhibited higher viability and improved hepatic functions compared to cells cultured on a noncoated or collagen type I-coated substrate. Also liver ECM hydrogels engineered with rat hepatocytes maintained the hepatic phenotype and functions after *in vivo* transplantation. Decellularized tissues have been used as a carrier for hepatocyte transplantation. This approach resulted in longer hepatocyte survival and higher metabolic activity compared to the infusion of unsupported hepatocyte suspensions.

An implantable engineered tissue represents a novel approach to overcome limitations of cell therapy and to provide small hepatic mass (<5%) to improve metabolic function. However, in order to replace the vital functions of a human liver and allow patient survival, a much larger mass (>25%) is needed. This ambitious goal is the core aim of the whole organ decellularization–recellularization technology that is covered in the next section.

CONCLUSION

The theory of an artificial liver support has been explain to be successful in animal studies. In addition, clinical application of an artificial liver devices has explain to be safe. Clinical analysis of an artificial liver treatment is severely inhibited by the variation in the patient groups studied and the fact that most patients undergo subsequent OLT. After treatment however, the neurologic and biochemical parameter improved with different artificial liver systems. To ultimately regulate the effect of an artificial liver treatment on survival, controlled, randomized clinical trials in large patient groups are required to produce statistically significant outcomes. An artificial liver research should also focus on the replacement of hepatocytes of animal origin by hepatocytes of human origin, either primary hepatocytes or immortalized cell lines, to overcome possible immunologic reactions and zoonosis.

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