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STEM CELL THERAPY IN PHARMACY: A BOLD STEP TO MAKE STEM OF RESEARCH ULTRASTRONG

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ABSTRACT
Stem cells represent a new treatment option in medicine and pharmacy. Stem cells have been increasingly used for the treatment of many diseases. In fact, they have spurred a new age of medicine called regenerative medicine. In recent years, regenerative medicine has become a new revolution in disease treatment, especially with the use of stem cell drugs. Stem cell drugs refer to live stem cell-based products that used as drugs for particular diseases. Unlike autologous stem cell transplantation, stem cell drugs are "off-the-shelf" products that are ready to be used without requirement of any further manipulation. This review aims to summarize some of the approved stem cell drugs, and discuss the revolution of regenerative medicine and personalized medicine. As well, the review will discuss how stem cell drugs have led to a new direction in stem cell therapy, providing a new platform for patient needs.

KEYWORDS: Adult Stem Cells, Mesenchymal Stem Cells, Haemetopoeitic Stem Cells, Embroynic Stem Cells, Totipotent, Pluripotent, Multipotent, Oligopotent, Unipotent.

INTRODUCTION
Stem cells represent a new treatment option in medicine and pharmacy. Stem cells have been increasingly used for the treatment of many diseases. In fact, they have spurred a new age of medicine called the regenerative medicine. In recent years, regenerative medicine has become a new revolution in disease treatment, especially with the use of stem cell drugs. A stem cell is a cell with the unique ability to develop into specialised cell types in the body. In the future they may be used to replace cells and tissues that have been damaged or lost due to disease. Our body is made up of many different types of cell. Most cells are specialised to perform particular functions, such as red blood cells; that carry oxygen around our bodies in the blood, but they are unable to divide. Stem cells provide new cells for the body as it grows, and replace specialised cells that are damaged or lost. They have unique properties that enable them to do this. They can divide over and over again to produce new cells. As they divide, they can change into the other types of cell that make up the body. There are three main types of stem cell: (a) embryonic stem cells (b) adult stem cells (c) induced pluripotent stem cells.[1]

EMBRYONIC STEM CELLS: Embryonic stem cells supply new cells for an embryo; as it grows and develops into a baby. These stem cells are said to be pluripotent, which means they can change into any cell in the body.

ADULT STEM CELLS: Adult stem cells supply new cells as an organism grows and to replace cells that get damaged. Adult stem cells are said to be multipotent, which means they can only change into some cells in the body, not any cell, for example: Blood (or 'haematopoietic') stem cells can only replace the various types of cells in the blood. Skin (or 'epithelial') stem cells provide the different types of cells that make up our skin and hair.

Embryonic and Adult Stem Cells.

INDUCED PLURIPOTENT STEM CELLS: Induced pluripotent stem cells, or 'iPS cells', are stem cells that scientists make in the laboratory. 'Induced' means that they are made in the lab by taking normal adult cells, like skin or blood cells, and reprogramming them to become stem cells.

Just like embryonic stem cells, they are pluripotent so they can develop into any cell type.

Stem cells have several uses including: (a) research – to help us understand the basic biology of how living things

work and what happens in different types of cell during disease. (b) therapy – to replace lost or damaged cells that our bodies can't replace naturally.[2]

STEM CELL RESEARCH: Research is looking to better understand the properties of stem cells so that we can: (a) understand how our bodies grow and develop (b) find ways of using stem cells to replace cells or tissues? that have been damaged or lost. We can use stem cells to study how cells become specialised for specific functions in the body, and what happens when this process goes wrong in disease. If we understand stem cell development, we may be able to replicate this process to create new cells, tissues and organs? We can grow tissue and organ structures from stem cells, which can then be studied to find out how they function and how they are affected by different drugs?

BEATING HEART CELLS: These heart cells were grown from stem cells in a petri dish and can be used to study the beating rhythm of the heart. Cells, tissues and organs can sometimes be permanently damaged or lost by disease, injury and genetic conditions?

Stem cells may be one way of generating new cells that can then be transplanted into the body to replace those that are damaged or lost. Adult stem cells are currently used to treat some conditions, for example:

Blood stem cells are used to provide a source of healthy blood cells for people with some blood conditions, such as thalassaemia, and cancer patients who have lost their own blood stem cells during treatment. Skin stem cells can be used to generate new skin for people with severe burns. Age-related macular degeneration (AMD) is an example of a disease where stem cells could be used as a new form of treatment in the future:
Some people with age-related macular degeneration lose their sight because cells in the retina? of the eye called retinal pigment epithelium (RPE) cells stop working. Scientists are using induced pluripotent stem cells to produce new RPE cells in the lab that can then be put into a patient's eye to replace the damaged cells.[3]

STEM CELL TREATMENT: An illustration showing how stem cells can be used to produce retinal pigment epithelium (RPE) cells that can be used to treat patients with age-related macular degeneration (AMD).

Stem cells could be used to generate new organs for use in transplants:
Currently, damaged organs can be replaced by obtaining healthy organs from a donor, however donated organs may be 'rejected' by the body as the immune system sees it as something that is foreign.

Induced pluripotent stem cells generated from the patient themselves could be used to grow new organs that would have a lower risk of being rejected. Signals in the body tell a cell what type of specialised cell it should be by switching some genes? on and some genes off. To generate induced pluripotent stem cells, scientists re-introduce the signals that normally tell stem cells to stay as stem cells in the early embryo. These switch off any genes that tell the cell to be specialised, and switch on genes that tell the cell to be a stem cell. Stem cells are defined as cells that have clonogenic and self-renewing capabilities and differentiate into multiple cell lineages. Stem cells are unspecialized cells that develop into specialized cells that make up the different types of tissues in the human body. They are vital to the development, growth, maintenance and repair of our brains, bones, muscles, nerves, blood, skin and other organs. While stem cell-based treatments have been established as a clinical standard of care for some conditions, such as haemopoietic stem cell transplants for leukaemia and epithelial stem cell-based treatments for burns and corneal disorders, the scope of potential stem cell-based therapies has expanded in recent years due to advances in stem cell research. It has been only recently that scientists have understood stem cells well enough to consider the possibilities of growing them outside the body for long periods of time. With that advance rigorous experiments can be conducted, and the possibility of manipulating these cells in such a way that specific tissues can be grown in real.[4]

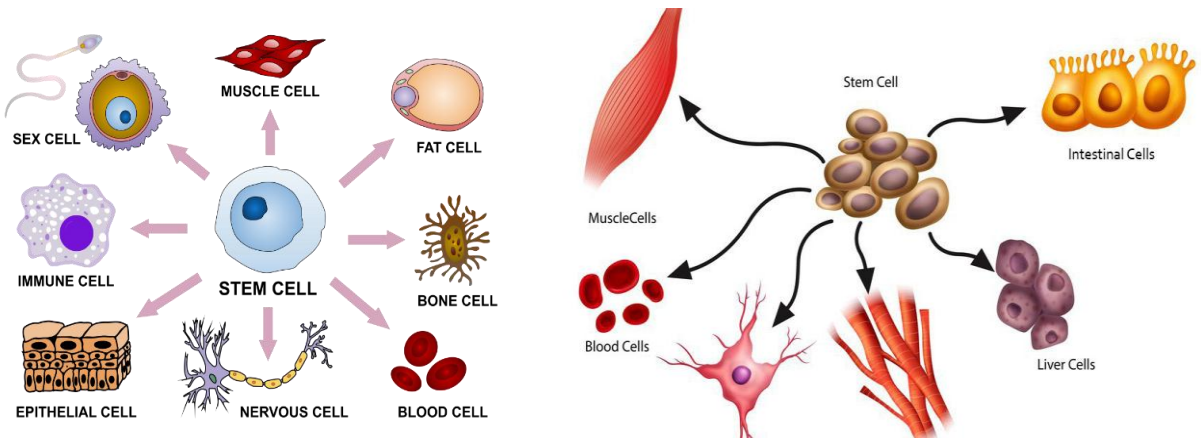

Figure-1: Stem cells.

TYPES: They are divided into two groups. They are-
ADULT STEM CELLS (ASCs): They are undifferentiated cells. More accurately they are called somatic stem cells because they can also come from foetuses, umbilical cords and infants. ASCs are believed to exist in small numbers in most tissues and organs including the bone marrow, liver, gut, blood and brain. They are called on during tissue repair to replace damaged cells. Two of the most researched subpopulations of bone marrow stem cells are:

MESENCHYMAL STEM CELLS (MSCs): They are non-haematopoietic, stromal calls that under appropriate stimuli, can differentiate into bone, cartilage, fat, tendon and muscle cells. Originally isolated from bone marrow and stroma of the spleen and thymus, MSCs have more recently been isolated from other sites including cartilage, periosteum, synovium, synovial fluid, blood vessels, muscle and tendon. However, it is not yet clear that till what extent MSCs are responsible for normal growth or maintenance *in-vivo*. MSCs are an attractive option for cell-based therapy because of their potential for autologous cell-based therapies and their relatively low immunogenicity.[5]

HAEMATOPOIETIC STEM CELLS (HSCs): They are stromal cells that can differentiate into all types of blood cell including platelets. Successful HSC transplant have been performed for a number of years using autologous bone marrow and allogenic umbilical cord to treat patient with no-malignant and malignant haematopoietic disorders such as leukaemia. However, such procedures are hampered by the rarity of these stem cells.

EMBRYONIC STEM CELLS (ESCs): They have only recently (1998) been isolated from human. ESCs are cultured from the undifferentiated inner mass cells of a blastocyst (an early stage embryo that consists of 50 to 150 cells). Once established, an embryonic stem cell line is immortal (ie. capable of continuous proliferation without differentiation). ESCs compared with the ASCs are more pluripotent and able to self-renew which makes them a versatile therapeutic option. ESCs, however cannot be used directly in cell therapies because they form tumours. The therapeutic potential of ESCs, therefore, relies on their directed differentiation into a particular specialised cell (eg. Insulin-producing β cells for diabetes), before administration.

According to differentiation potential stem cells can be divided into 5 types:
TOTIPOTENT: The ability to differentiate into all possible cell types. Eg. are the zygote formed at egg fertilization and the first few cells that result from the division of the zygote.

PLURIPOTENT: The ability to differentiate into almost all cell types. Eg. include embryonic stem cells and cells that are derived from the mesoderm, ectoderm, endoderm germ layers that are formed in the beginning stages of embryonic stem cell differentiation.

MULTIPOTENT: The ability to differentiate into a closely related family of cells. Eg, include haematopoietic (adult) stem cells that can become red and white blood cells or platelets.

OLIGOPOTENT: The ability to differentiate into a few cells. Eg. include (adult) lymphoid form myeloid stem cells.

UNIPOTENT: The ability to produce cells of their own type, but have the property of self-renewal required to be labelled a stem cell. Eg. include (adult)muscle stem cells.[6]

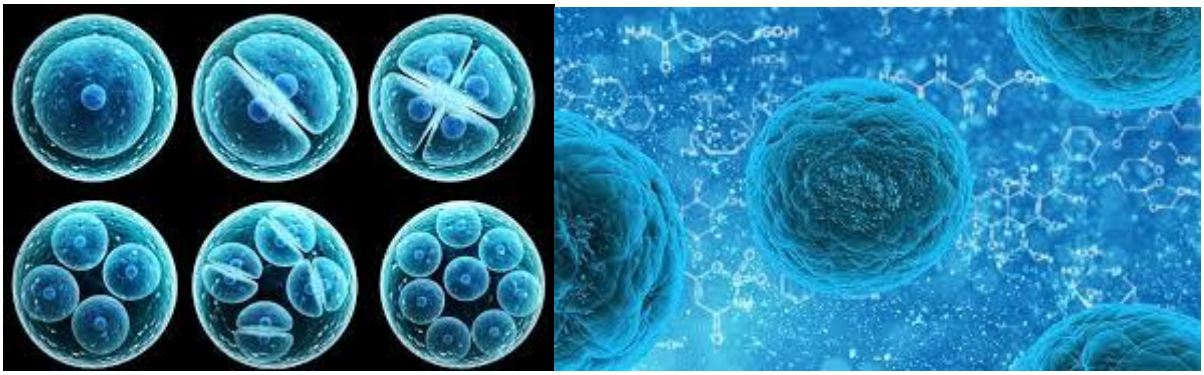

Figure-2: Scanning Electron Micrograph of Stem Cells.

TIMELINE OF MAJOR ADVANCES IN STEM CELL RESEARCH
1907-European scientists realise that all blood cells come from one *stem cell*.
1963-Bone marrow injected into irradiated mice is found to be able to self-renew and differentiate.
1968-The first bone marrow transplant (adult stem cells) is successfully used to treat severe combined immunodeficiency disorder.
1972-Mouse teratoma (a tumour containing tissues derived from all embryonic layers) cell line is established.
1981-A pluripotent mouse cell line is established.

1996-The first mammal (Dolly the sheep) is cloned using ASCs using somatic cell nuclear transfer.
1998-A pluripotent human cell line is established.
2003-Oocytes from the mouse embryonic stem cells are derived, demonstrating that ESCs can be totipotent.
2004-The world's first stem cell bank opens in UK to store, characterise and supply ethically approved, quality-controlled cell lines for research and ultimately, treatment.
2004-A human embryonic stem cell line from an adult (somatic) cell isolated from a living person is generated. This might allow ESC therapies or regenerative medicine with patient's own DNA, preventing immune rejection.
2005-A new technique to extract ESCs without damaging the embryo is developed.
2005-A new human embryonic stem cell line, free from any animal components is created. (Existing human embryonic stem cell lines used animal cells and serums for culture, which could present human health risks.
2005-World human embryonic stem cell bank is established in South Korea. This may help scientists avoid government restrictions on cloning.
2006-First successful cloning of human embryo to make stem cells.
2007-First evidence for human colon cancer stem cells.
2007-First physical identification and localization of mammalian intestinal stem cells.
2008-Scientists created stem cells for 10 disorders.
2009-Stem cell transplant reported to be promising treatment for curing HIV.
2009-Stem cell transplants reported to improve survival for leukaemia patients.
2010-First clinical trial for human embryonic-derived stem cells for treatment of spinal cord injuries.
2011-First safety trial launched in humans to test embryonic stem cell therapy to treat blinding diseases.
2014-Breakthrough for manufacturing stem cells.
2014-First embryonic stem cells cloned from a man's skin.
2015-First UK patient received experimental stem cell treatment for age-related macular degeneration.
2016-Scientists announce the first generation of an embryonic stem cell that carries a single copy of the human genome rather than the usual two.
2017-Gene therapy reported to successfully reverse sickle cell disease in first patient.
2018-Mouse and human skin cells reprogrammed into immune cells to fight cancer.
2019-Gene therapy shown to be promising in treating infants born with X-linked severe combined immunodeficiency (SCID-X).

Figure-3: Embryonic Stem Cells.

WHAT ARE STEM CELL DRUGS? Stem cell drugs are new members of stem cell therapy, personalized medicine and regenerative medicine. The development of stem cell drugs has impacted and advanced stem cell industry as well as pharmaceutical industry. They are off-the-shelf products; stem cell drugs are used in the allogenic setting stem cell transplantation. There are key differences between allogenic stem cell transplantation and stem cell drugs. The stem cell drug is a product, while allogenic stem cell transplantation is a procedure using the stem cell drug. Moreover, the former is approved as a drug and the latter is approved as a medical device.[7]

STEM CELL DRUGS: FROM PERSONALIZED TO UNIVERSALIZED: Personalized medicine is a medical procedure that separated patients into different groups-with medical decisions, practices, interventions and/or products being tailored to the individual patient based on their predicted response or risk of the disease. Stem cells offer a new approach in personalized medicine. Stem cell drug for universalized medicine has become a new option in stem cell therapy. Stem cell drugs can overcome all the major limitations of autologous stem cells. Particularly, the quality, quantity and price can be controlled.

While personalized medicine requires more time for development and is, in some ways, a form of medicine for the 'future', universalized medicine is more 'real' in that the 'off-the-shelf', allogenic stem cell drugs can be used for many patients.

STEM CELL DRUGS: DRUG MECHANISM AND PROPERTIES: Stem cell drugs are mainly produced from HSCs and MSCs. However, another kind of stem cell (limbal stem cells) can also be used to produce some products for corneal regeneration. The mechanisms of action these stem cells drugs are different. While HSC based drugs can regenerate the haematopoietic system in treated patients (via homing and differentiation functional cells), MSC based drugs typically target the immune system and facilitate healing at injured sites by paracrine or endocrine factors.

PROCESS OF STEM CELL THERAPY: The first part of the stem cell transplant process is called conditioning. During this time, patient receives chemotherapy and/radiation therapy and/or full body irradiation therapy to damage and possibly destroy the bone marrow. The stem cell transplant itself replaces the damaged bone marrow with healthy stem cells. Stem cell transplantation is more as a transfusion of blood and immune cells procedure rather than a surgical procedure. Bone marrow is replenished after very high doses of treatment for the blood count to recover. The type and source of stem cell in this process is based on the type of disease to be treated.[8]

WHO WILL GET BENEFIT FROM STEM CELL THERAPY RESEARCH?

HEART DISEASE: Heart disease is the leading cause of death in developed countries. Clinical studies suggest that adult stem cells may benefit heart conditions, including myocardial infarction and advanced heart failure. Stem cell repopulation of damaged myocardial tissue by trafficking bone marrow stem cells into the circulation using cytokine during treatment is promising.

NEURODEGENERATIVE DISORDERS: Parkinson's disease currently afflicts, respectively, 110,000 and over 500,000 people in UK. Neural stem cells found to reside throughout the central nervous system have been shown to differentiate into neuronal cells when transplanted aged rat brains, significantly improving cognition. Neuronal embryonic stem cells, directed to differentiate into neurons and transplanted into brains, have been shown to cause neurogenesis in mouse disease models.

DIABETES: An estimated 415 million people worldwide have diabetes, with numbers predicted to rise up to 642 million worldwide by 2040. ASCs isolated from the pancreas, liver and bone marrow, and transplanted into the pancreas of a patient suffering from diabetes have been shown to differentiate into islet-like clusters that produce insulin. In some mouse models glycaemic control can be achieved.

ORTHOPAEDIC DEFECTS AND JOINT DISEASE: About 150 million people suffer from some form of arthritis worldwide. Autologous, *ex-vivo* expanded bone marrow osteoprogenitor cells transplanted into patients with large bone defects show good initial osteointegration and promote full limb recovery within 12 months. When mesenchymal stem cells were injected into osteoarthritic goats, further cartilage destruction was retarded and meniscus regenerated.

SKIN REPLACEMENT: The knowledge of stem cells has made it possible for scientists to grow skin from a patient's plucked hair. Skin (keratinocyte) stem cells reside in the har follicle and can be cultured to form an epidermal equivalent of the patient's own skin and provides tissue for an autologous graft, bypassing the problem of rejection.

BRAIN CELL TRANSPLANTATION: Stem cells provide dopamine; a chemical lacking in victims of Parkinson's disease. It involves the loss of cells which produce the neurotransmitter dopamine. The first double-blind study of foetal cell transplants for Parkinson's disease reported survival and release of dopamine from the transplanted cells and a functional improvement of clinical symptoms. However, some patients developed side effects, which suggested that there was an over sensitization to or too much dopamine. Although the unwanted side effects were not anticipated, the success of the experiment at the cellular level is significant.[9]

REBUILDING THE NERVOUS SYSTEM WITH STEM CELLS: The past decade has seen impressive advances in the prevention and treatment of cerebrovascular disease. Several new therapies are under investigation to address the long-term disability of stroke survivors. Stem cell therapy offers exciting potential for ambitious cellular replacement to treat diseases such as Parkinson's disease, Alzheimer's disease or even replacement of the cell death that follows thromboembolic stroke. Longer-term safety and efficacy results should enhance our understanding of cell implantation therapy for the treatment of stroke.

SPINAL CORD DISORDERS: Clinicians and scientists in the field of spinal cord injury research and medicine are poised to begin translating promising new experimental findings into treatments for people. Advances in stem cell research have to several transplantation strategies that promote axonal regrowth and partial functional recovery in spinal cord injury.[10]

STEM CELL THERAPY FOR HIV: The haematopoietic stem cell has long been hypothesized to be a target of human immunodeficiency virus type-1 (HIV) infection that limits the potential for compensatory immune cell production. Data have recently emerged documenting stem cell dysfunction in HIV disease and indicating the immune recovery from potent antiretroviral therapy is partly driven by new T-cell generation. Effects of HIV on stem cell physiology, however, appear to be indirect, as stem cells are highly resistant to HIV infection. Despite the presence of surface receptors for HIV, the haematopoietic stem cell

is not infectible with HIV and can serve as a resource for cellular therapies for AIDS.[11]

PULMONARY MEDICINE: Cystic fibrosis, idiopathic pulmonary degeneration, lung transplantation are the recent areas of pursuit.

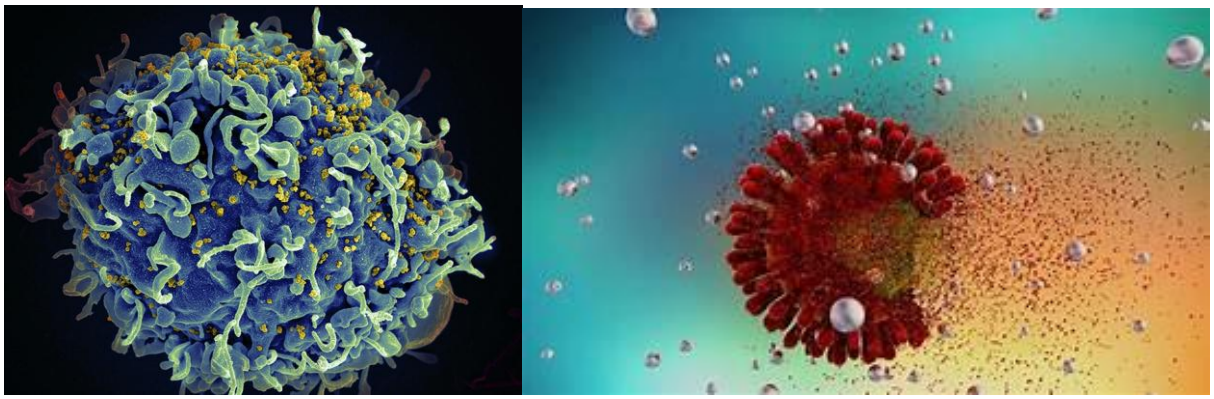

Figure-4: HIV Stem Cells.

OPTHALMOLOGY: Stem cells hold promise to retinal degeneration, glaucoma and corneal disorders.

HOW STEM CELL TRANSPLANTS WORK AGAINST CANCER? Stem cell transplants do not usually work against cancer directly. Instead, they help to recover the ability to produce stem cells after treatment with very high doses of radiation therapy, chemotherapy or both. However, in multiple myeloma and some types of leukemia, the stem cell transplant may work against cancer directly. This happens because of an effect called graft-versus-tumour that can occur after allogenic transplants. Graft-versus-tumour occurs when white blood cells from the donor (the graft) attack aby cancer cells that remain in the body (the tumour) after high dose treatments. This effect improves the success of the treatments.[12]

FUTURE OF STEM CELL THERAPY: In recent years, stem cell therapeutic studies has progressed from use of whole stem cells to components derived from stem cells. The components have included stem cell extracts, micro-vesicles and exosomes, all of which exhibit various biological activities. The new discoveries suggest the dawn of new era of stem cell therapy, i.e stem cell drugs. Here, components (mRNA, protein and peptides) from stem cells, in micro-vesicles or exosomes, can be effective over whole stem cells. Certainly, the advantages of stem cell drugs include reduction of immunogenicity and easy processing, storage and delivery. Stem cells free drugs may play a potentially important and emerging role in regenerative medicine.[13]

OVERVIEW: Recent research advances in the understanding of stem cell properties are inevitably leading to therapeutic strategies potentially applicable to many diseases. The pharmaceutical manipulation of multipotential cells such as stem cells is therefore now primed to evolve in its own right. This article focuses on known effects of introduced biologics and small molecules, and on the future of strategies enhancing the *ex-vivo* or *in-vivo* regenerative properties of these remarkable cells. Therapies targeting multipotential cells offer hope to treat many degenerative diseases caused by the premature death or malfunction of specific cell types. With a lack of suitable pharmaceutical treatments and long waiting lists for transplantable organs, such cell-oriented approaches are being advanced based on either the introduction of cells into patients (*ex-vivo* cell therapies) or the use of agents to affect cells already within the patient (*in-vivo* therapies). It is an emerging area of biotechnology taking advantage of research advances in fields such as cell signalling and the use of 3 growth factors to repair damage caused by disease, trauma and processes such as ageing. Therapies targeting multipotential cells address numerous large healthcare markets by promising novel therapies to treat debilitating diseases such as diabetes, Parkinson's, Huntington's, heart disease and stroke, as well as accidental damage such as spinal cord injury. They are emerging as a potentially revolutionary way to treat malignancies, blood disorders, as well as certain inborn errors of metabolism and immunodeficiencies. Replacement of the blood and immune systems with blood stem cells, the use of neural stem cells to treat neurodegenerative systems, the use of mesenchymal stem cells to repair bones and joints and liver stem cells for liver failure are just a few examples of clinical applications of endogenous multipotential cell targeted therapies. About stem cell. A drug is defined as any substance other than food that when inhaled, injected, smoked, consumed, absorbed via a patch on the skin or dissolved under the tongue causes a physiological change in the body. In pharmacology, a drug (or pharmaceutical drug) is a substance used to treat, cure, prevent or diagnose a disease or to promote well-being. According to this definition, a drug must satisfy some criteria, such as having indication to treat any disease and is an off the-shelf product. Therefore, by definition stem cell drugs are off-the-shelf products based on stem cells that are indicated to treat, cure, prevent or diagnose a disease or to promote well-being. According to this definition, a drug must satisfy some

criteria, such as having indication to treat any disease and is an off-the-shelf product. Therefore, by definition stem cell drugs are off-the-shelf products based on stem cells that are indicated to treat, cure, prevent or diagnose a disease or to promote well-being. As off-the-shelf products, stem cell drugs are used in the allogeneic setting in stem cell transplantation. There are key differences between allogenic stem cell transplantation and stem cell drugs. The biggest difference between them is that the stem cell drug is a product, while allogenic stem cell transplantation is a procedure using the stem cell drug. Moreover, the former is approved as a drug and the latter is approved as a medical device. Mechanism and properties. Stem cell drugs are mainly produced from HSCs and MSCs. However, another kind of stem cell (limbal stem cells) can also be used to produce some products for corneal regeneration. The mechanisms of action of these stem cell drugs are different. While HSC based drugs can regenerate the hematopoietic system in treated patients (via homing and differentiation to functional cells), MSC based drugs typically target the immune system and facilitate healing at injured sites by paracrine or endocrine factors. Hematopoietic stem cell-based drug. HSCs are stem cells that can produce blood cells, including white blood cells, red blood cells and platelets, through the process of haematopoiesis. In adults, HSCs are located in the bone marrow and maintain the blood system in the body. The definition of HSC has evolved since the time HSCs were first discovered in 1961. Nowadays, HSCs are found in and mostly isolated from bone marrow, peripheral blood and umbilical cord blood. The first successful bone marrow derived HSC transplantation was performed in 1950s by E. Donnall Thomas at Fred Hutchinson Cancer Research Centre (Washington, USA); his work was later recognized with a Nobel Prize in Physiology or Medicine. The roles of HSCs in both malignant and non-malignant diseases were determined by homing and differentiation of HSCs at bone marrow to form a new haematogenesises system. However, HSCs exert strong immunogenicity on the host immune system. Therefore, HLA matching is critical prior to HSCT. The requirement of HLA matching, however, restricts the development and advancement of HSC based stem cell drugs since there is extremely low HLA matching in the human population. Moreover, it is difficult to induce stem cell proliferation in vitro to increase cell quantity. Mesenchymal stem cell drug therapy. Mesenchymal stem cells (MSCs) are the most popular stem cells in the human body. They are present in almost all tissues but the most common sources are bone marrow, adipose tissue, umbilical cord tissue, umbilical cord blood, and placenta. Unlike other kinds of stem cells, MSCs are multifunctional; they not only differentiate into multiple cell lineages but they also produce a pool of cytokines and growth factor to execute immune modulation and promote injury healing and tissue regeneration. MSCs are favourable for clinical applications of stem cell therapy due to their multiple lineage differentiation potential. Stem cells can be differentiated *in-vitro* or *in-vivo* into functional cells which can replace aged or damaged cells. Indeed, some applications of stem cell therapy have entailed differentiating cells from stem cells *in-vitro* and then transplanting them into the recipient as cellular therapy or in combination with biomaterials as tissue engineering therapy. In stem cell transplantation, scientists are also evaluating and trying to promote *in-vivo* differentiation in the microenvironment. Ideally, stem cells can home to injured tissue sites in the body and persist for a long time. Persistence of stem cells has been observed in HSC transplantation and, in some cases, in autologous MSC transplantation. Indeed, in MSC transplantation more than 50% of grafted cells typically die in the recipient from rejection by the immune system and selection in the microenvironment. Autologous transplantation or HLA matching, therefore, are necessary to overcome the kinds of challenges. MSCs were used as the source for stem cell-based drugs. The two main mechanisms of therapy mediated by stem cell drugs are immune modulation and paracrine/ endocrine effects. Immune modulation is the most common mechanism of commercialized stem cell drugs generated nowadays; about 80% of stem cell drug products act via immune modulation. This means that the host immune system can be regulated by either indirect or direct interactions between stem cells and host immune cells. The second main mechanism of stem cell drugs relates to the growth factors produced by stem cell. The future of stem cell. In recent years, stem cell therapeutics studies have progressed from use of whole stem cells to components derived from stem cells. These components have included stem cell extracts, macrovesicles and exosomes, all of 10 which exhibit various biological activities. For example, exosomes from MSCs have functions similar to whole MSCs, including repair of tissue damage, suppression of inflammatory responses, and modulation of the immune system. Exosomes from stem cells can also affect other systems and organs, such as the cardiovascular system, kidney, liver, nervous system and musculoskeletal system. In kidney, studies have shown that acute kidney injury can be effectively treated with MSC based exosomes. MSC derived exosomes have been evaluated in the treatment of neurological and neurodegenerative diseases; they have been shown to enhance angiogenesis and neurogenesis, reduce inflammation and improve spatial learning and sensorimotor function. Stem cells free drugs may play a potentially important and emerging role in regenerative medicine.[14]

REMAINING RESEARCH HURDLES: Several hurdles remain before the enormous potential of stem cells can be realised. These include greater efficiency in ESC isolation and in establishing embryonic stem cell lines, overcoming immunogenic issues, and the characterisation of stem lines using sophisticated genetic and proteomic technologies. There is also a need for the greater standardisation of techniques and procedures to ensure accurate reproduction of studies. Further limiting use of animal products in stem cell culturing methods

will help to improve the immunogenic health risks associated with contaminated stem cells.

Research in dedifferentiation of ASCs is also vital. However, the most significant hurdle in stem cell research is the identification of the signals that determine the differentiation and the signals that inhibit activity after injury repair. The progress of stem cell research has been evident by the shift of focus from broader questions concerning stem cell potency and regeneration potential to more specific biological questions regarding stem cell survival and capacity to populate host tissues as well as their effectiveness after topical implantation and circulation.

CONCLUSION

Stem cell drugs are new members of pharmaceutical medicines that are produced from stem cells. From 2012 to now<more than ten stem cell drugs have been approved in various countries for clinical applications. These products may contain live haematopoietic stem cells or mesenchymal stem cells. With their advantages such as decreased immunogenicity and ease of processing<stem cell drugs have emerged as a promising new platform in the field of stem cell therapy around the world. As a new product pf pharmaceutical medicine, it is anticipated that stem cell drugs will significantly contribute to both medical and pharmaceutical industries in the near future. In clinical applications, beside the stem cell drugs which contain live and whole stem cells, new stem cell drugs containing components from stem cells (such as extracts, exosomes and vesicles) are in development and expected to be launched soon.

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