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Review article Therapeutics

Lipid based nano therapeutics

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ABSTRACT

In recent years, various nanotechnology platforms in the area of medicinal biology, including both diagnostic and therapy, have gained remarkable attention. Nanotechnology offers many advantages in the field of science. The development of nanoparticle-based drug formulations has yielded the opportunities to address and treat challenging diseases, and also have proven that nanoparticles acquire a great potential in medical applications. The different types of nanoparticles include carbon-based nanoparticles, ceramic nanoparticles, metal nanoparticles, polymeric nanoparticles and lipid based nanoparticles. Nanoparticles combine with the therapeutic agents to overcome the problems associated with combination therapy, photodynamic therapy and are well concerned before their usage in biological systems. Nanoparticles vary in their size but range from 100-500nm. We provide an overview of new clinically used nanoparticles and their therapeutic specificity for treating various diseases. We foreground current delivery programmes for specific diseases such as diabetes, cancer (to target myeloma), cardiovascular disorders, neurological disorders, HIV/AIDS, as well as many types of inflammatory and infectious diseases and also providing the evolution in diagnostic testing.

Keywords: Nanoparticles, diabetes, wound healing, foot ulcers.

INTRODUCTION

Nanomedicine is an upcoming approach for the implementation of nanotechnology in diagnosis and therapy. This is the branch of medicine that is concerned with the use of nanotechnology. Nanomedicine branch of nanotechnology is grouped into 3 interrelated areas: analytical / diagnostic tools, drug delivery and regenerative medicine. Nanomedicine can be classified into 2 two main types: nanodevices and nanomaterials. Nanotechnology is a branch of technology that deals with dimensions and tolerances of less than 100 nm, especially the manipulation of individual atoms and molecules. Nanotechnology is one of the most auspicious technologies of the 21st century. It is the ability to convert the nanoscience theory to useful applications by observing, measuring, manipulating, assembling, controlling and manufacturing matter at the nanometer scale. These efforts are further aided by the creation of outstanding excellence centres and other initiatives by the National Institutes of Health (NIH), including a national network of eight nanomedicine development centres, which serve as the intellectual and technological centrepiece of the NIH Nanomedicine Roadmap Initiative.

HISTORY

The American physicist and Nobel Prize laureate Richard Feynman introduced the concept of nanotechnology in 1959. During the annual meeting of the American Physical Society, Feynman presented a lecture entitled "There's Plenty of Room at the Bottom" at the California Institute of Technology. After fifteen years, Norio Taniguchi, a Japanese scientist was the first to use and define the term "Nanotechnology" in the year 1974 as: "nanotechnology mainly consists of the processing of separation, consolidation, and deformation of materials by one atom or one molecule".[1] K. Eric developed and popularized the

concept of nanotechnology and founded the field of molecular nanotechnology.

DEVELOPMENT & FORMATION OF NANOPARTICLES FOR THERAPEUTICS

The advancement of drug delivery systems has been proposed by the traditional clinical diagnostic methods to increase the drug specificity and diagnostic accuracy. Free nanoparticles are formed from the larger particles by breaking them into small pieces by controlled assembly process. In recent years, nanoparticles are engineered for advanced technologies and consumer products have become a new source of exposure. Various methods for preparation of nanoparticles were used such as: gamma radiation, thermal decomposition, chemical reduction, photochemical method, microwave irradiation. Nanoparticles have proved their promising effect on the development of clinical gene therapy because of their size, shape, surface and biological behaviours. In Magnetic Resonance Imaging (MRI) the contrast effect of nanoparticles depend upon their magnetic properties, which can be controlled by change in size and composition. [4]

IMPORTANCE OF PARTICLE SIZE

Nanoparticles are usually distinguished from micro particles, fine particles(sized between 100 and 2500 nm),because their small size drives very different physical or chemical properties, like colloidal properties and ultrafast optical effects.[5] Particle size reduction helps in enhancing the exposure of poorly soluble oral drugs by increasing the surface area and increasing the dissolution rate.[6] Particle size analysis is a key element in the pharmaceutical development, especially for products containing nano sized API. A wide range of techniques are available to determine the particle size such as:

- Sieves
- Sedimentation
- Electronic testing
- Laser Diffraction

The measurement of particle size is vital to ensuring product bioavailability, efficacy and shelf life since particle size influences the surface area and porosity. When developing the new pharmaceutical drugs, particle size analysis is one of the most important parameters to assess. Particle size analysis is done in every aspect of production such as:

- In case of building materials
- In paints and coatings etc…,

TYPES OF LIPID BASED NANOPARTICLES

Lipid based nanoparticles are subdivided into following types depending on their structure such as:

Liposomes: Liposomes are closed vesicles composed of a phospholipids bilayer and water soluble drugs can be incorporated into their aqueous phase, whereas lipid soluble drugs can be incorporated into their lipid phase.[7]

Lipid Nano emulsions: Nano emulsions are droplets with hydrophobic liquid core composed of the oil that is dispersed in the water and stabilized by a surfactant monolayer.

Solid lipid nanoparticles: These are submicron colloidal carriers ranging from 50-1000nm, which are composed of a physiological lipid dispersed in water or in aqueous surfactant solution.

Lipid nanoparticles: Lipid nanoparticles are spherical vesicles made of ionizable lipids, which are positively charged at low pH and neutral at physiological pH

Nano structured lipid carriers: These are novel pharmaceutical formulations which are composed of physiological and biocompatible lipids, surfactants and co-surfactants.

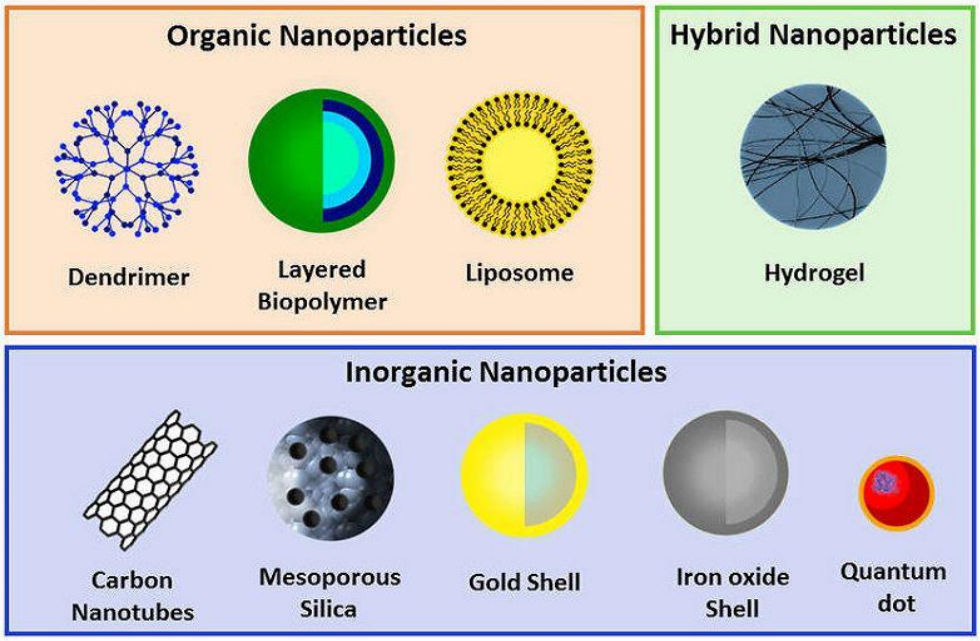


Fig 1: Types of Nanoparticles

USE OF NANOTECHNOLOGY FOR DIAGNOSTICS

- Quantum dots
- Nano shells
- Nano pyramids
- Nano gels
- Nano wires

These are used in diagnosis and treatment of gastrointestinal disorders, cancer therapy, diabetes, neurological disorders, cardiovascular disorders, and HIV/AIDS.

Nano diagnosis is defined as the use of nanotechnology for clinical diagnostic purposes which were developed in 1998 by Jain to meet the demands of clinical diagnostics for increased sensitivity and earlier detection of diseases.

APPLICATIONS

Cancer therapy

Cancer is the leading cause of death and global health burden. Cancer is defined as a disease caused by uncontrolled division of abnormal cells in any part of the body. The cancer therapy is limited to surgeries, radiation and chemotherapy. By using these therapies there will be damage to cancerous cells along with the normal healthy cell even though there will be incomplete eradication of the cancer from the body. Nano technology has created a promising development in nanotechnology by using its tools such as:

- Liposomes
- Polymeric micelles
- Quantum dots etc…,

Cardiovascular therapy

Nano technology can increase the efficiency of drugs, improve the local and systemic delivery to atherosclerotic plaques and reduce the inflammatory response after intra vascular intervention. As cardiovascular diseases (CVD) increasingly claim a number of lives globally, we propose more attention should be placed by researchers on nanotechnological approaches for risk factor treatment to aid in early prevention and treatment of CVD. Nanostructures systems have the potential to revolutionize both preventive and therapeutic approaches for treating cardiovascular disease. The tools used for testing the cardiovascular disorders include:

- Electrocardiogram
- Holter monitoring
- Echocardiogram
- Stress test
- Cardiac catheterization
- Cardiac computerized tomography
- Cardiac magnetic resonance imaging etc…,

HIV/AIDS therapy

Currently there is no cure for HIV/AIDS. Once you have the infection, the body cannot get rid of it. Combination antiretroviral therapy has dramatically improved the treatment. Nanotechnology has a vast potential to radially advance the treatment and prevention of HIV/AIDS. Highly active antiretroviral therapy which involves combination of at least three antiretroviral drugs has been used to extend the life span of HIV/AIDS patients. Nano technology has proven to have potentials of advancing the prevention and treatment of the viral agents. The nanotechnology used in treatment of HIV/AIDS includes:

- Nanotechnology antiretroviral drug delivery
- Nano materials as therapeutic agents

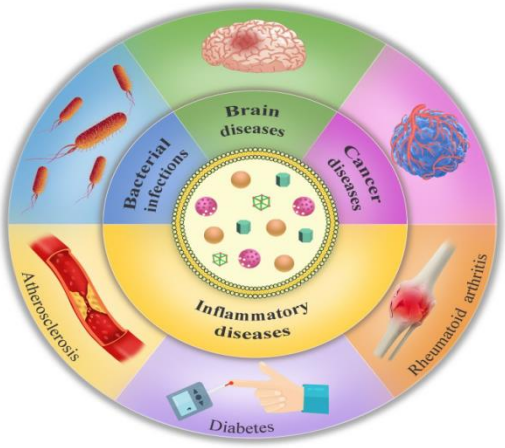
A nanoparticle is a small particle that ranges its size between 1 to 100 nm.

Nano materials are usually considered to be the materials with at least one external dimension that measures 100 nm or less or within internal structures measuring 100 nm or less.

Diabetes therapy

Diabetes mellitus is defined as the metabolic disorder increasing the blood glucose level in the body. The prevention and treatment of diabetes mellitus and its subsequent complications have brought trouble to human beings. Nano technology holds significant potential for improving the care of diabetes patients. Nanotechnology has proven beneficial in treating diabetes mellitus by not only improving the catalytic properties of the electrodes but also by increasing the available surface area of the sensor-receptor complex. The nano technology therapies involved in diagnosis of diabetes include:

- Insulin patch
- Insulin nanogel
- Cellular therapies



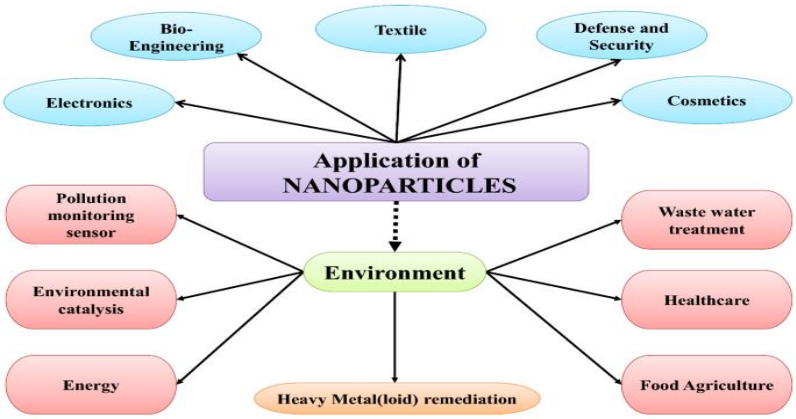


Fig 2: Applications of nanoparticles

DIABETIC WOUND HEALING

Diabetic mellitus is defines as a syndrome characterized by hyperglycemias resulting from impaired insulin secretion, associated with the risks of diabetic ketoacidosis (DKA) and a group of late complications including retinopathy, nephropathy, atherosclerotic coronary and peripheral arterial disease and peripheral and autonomic neuropathies. Diabetes affects approximately 170 million people worldwide, including 20.8 million in the USA. [2] National Diabetes Statistics fact sheet. Out of 62 million diabetics in India, 25% develop Diabetic foot ulcers, of which 50% get infected, requiring hospitalization while 20% need amputation. It is projected that the annual global health expenditure on Diabetes mellitus in 2019 is USD 760 billion, which will reach USD 825 billion by 2030. [3]

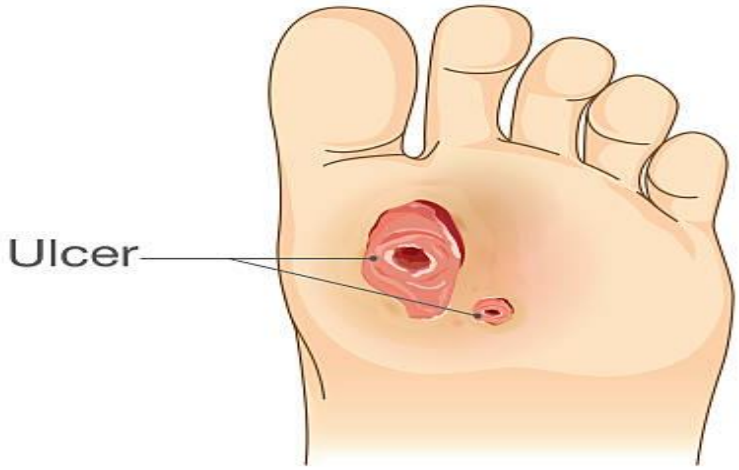


Fig 3: Diabetic wound healing

PATHOPHYSIOLOGY OF DIABETIC WOUND HEALING

There are 4 basic phases of wound healing:

1. Haemostasis phase
2. Inflammatory phase
3. Proliferative phase
4. Maturation or remodelling phase

HAEMOSTASIS

Haemostasis is the first phase of healing. Haemostasis is the process that starts or begins at the onset of injury and stops the bleeding. In this phase the body activates its emergency repair system which includes blood clotting factors. This helps in the formation of clots. The platelets released during this process attach to the collagen that is present in the injured area and carry the collagen to the platelets and then they release some of the mediators like thromboxane A2, phospholipase A2, cyclooxygenase 1. The thromboxane forms thrombin from Prothrombin and initiates the formation of fibrin clots at the injured area, which strengthens the platelet lumps into stable clots.

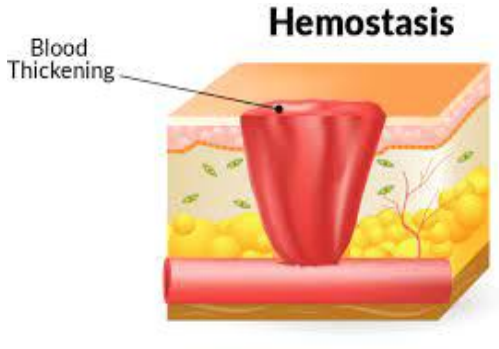


Fig 4: Haemostasis phase

INFLAMMATORY PHASE

Inflammation is the second phase of wound healing and begins right after the injury. It involves phagocytic cells that release reactive oxygen species, lasting up to 7 days, in acute wounds and lasts longer in chronic wounds. During this phase, white blood cells and some enzymes enter the wound area to stave off infection by clearing bacteria and debris and preparing the wound bed for new tissue growth. Physical characteristics of the wound include inflammation, redness at the site of wound, oedema, heat and pain.

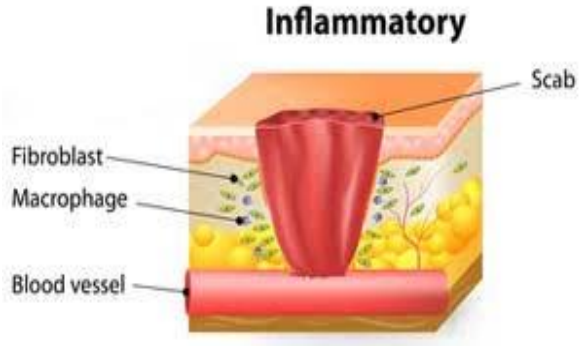


Fig 5: Inflammatory phase

PROLIFERATIVE PHASE

In this phase, the wound contracts as the new tissues are built. In addition to it a new network of blood vessels must be constructed so that granulation tissue receives sufficient oxygen and nutrients. Myofibroblasts cause the wound contract by gripping the wound edges and pulling them together. In the final stage of the proliferative phase of wound healing, epithelial cells resurface the injury. It is important to make sure that epithelialization happens faster when the wound is kept moist and hydrated. When occlusive dressings are applied within 48hrs after injury, they will maintain correct tissue humidity to optimize epithelialization.

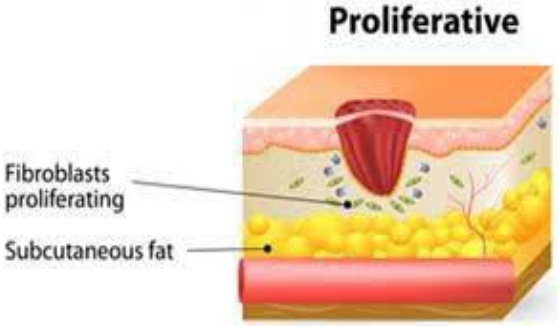


Fig 6: Proliferative phase

MATURATION PHASE

This phase is also called the remodelling phase. In this phase the collagen is remodelled and the wound is fully closed. The cells that have been used to repair the wound but which are no longer needed are removed by apoptosis process. Collagen is remodelled along the organized tension lines, thereby increasing the tensile strength of the healing tissues. Generally, remodelling begins after 21 days of an injury and can continue over for a year or more.

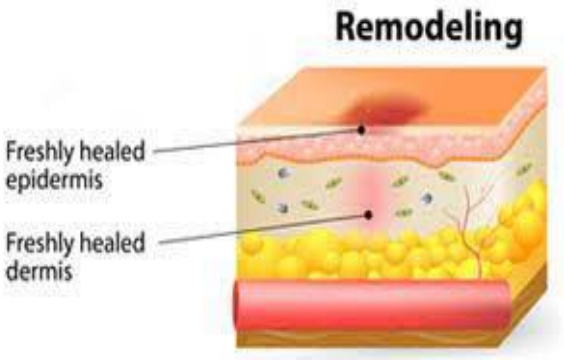


Fig 7: Remodelling phase

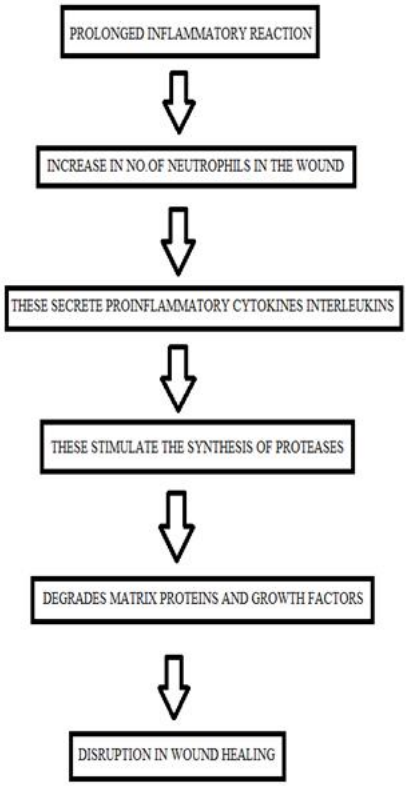
DIABETIC WOUND HEALING PROCESS

Minor wounds, cuts, and burns are an unfortunate but unavoidable part of life. However, for people with diabetes, these injuries can lead to serious health issues. Many people with diabetes develop wounds that are slow to heal, do not heal well, or never heal. If an untreated wound becomes infected, then the infection may spread locally to muscles and bones. A small wound on the foot can quickly develop into a foot ulcer. Foot ulcers can become serious if left untreated. About 15% of people who have diabetes develop foot ulceration.

WHY WOUND HEALING IS SLOW

- High blood sugar level
- Neuropathy
- Poor circulation
- Immune system deficiency
- Infection

PROCESS OF DIABETIC WOUND HEALING



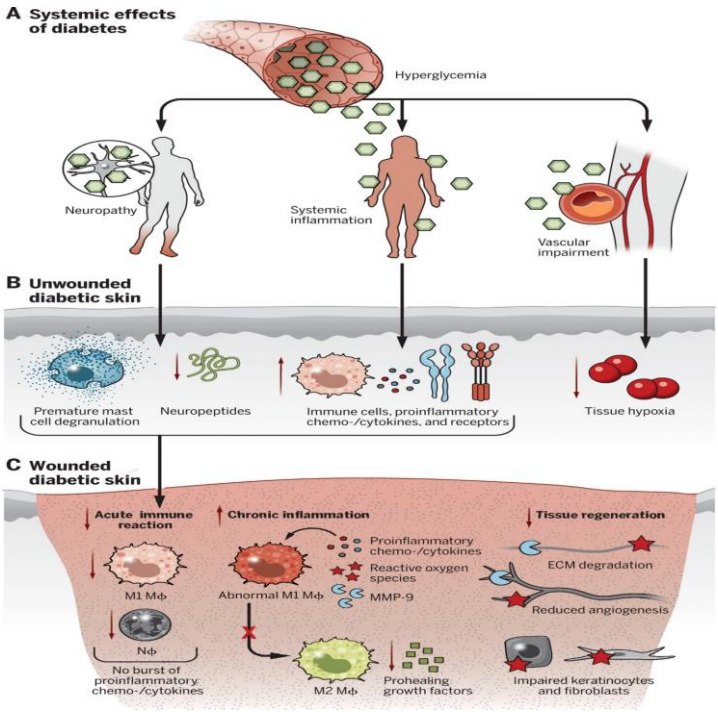


Fig 8: A diagram explain the difference between normal wound healing and diabetic wound healing

The underlying causes include:

- Poor glycemic control
- Foot deformities
- Improper foot care
- Peripheral neuropathy
- Poor circulation
- Dry skin etc…,
- **Poor circulation** is a form of vascular disease in which blood doesn't flow to your feet efficiently. Poor circulation can also make it more difficult for ulcers to treat.
- **High glucose levels** can slow the healing process of an infected foot ulcer, so blood sugar management is critical.

REASONS FOR DIABETIC WOUND HEALING

The 3 main reasons for diabetic wound healing include:

- Neuropathy
- High blood sugar
- Reduced immune system function

PREVENTION OF FOOT ULCERS

1) Check your feet daily
2) Don't walk around barefoot
3) Wear shoes that fit properly
4) Get right nutrients
5) Suspicious? Consult doctor.

TREATMENT

Non-healing wounds results in enormous health care expenditure, with the total cost estimated at more than $3 billion per year.[8] Non-healing chronic wounds are diabetes, venous or arterial disease, infection and metabolic deficiencies of old age.[9]

1. Dressing
2. Anti-diabetic drugs
3. Growth factors
4. Stem cell therapy
5. Nanotechnology

DRESSING

The ideal wound dressing should be nonallergic and nontoxic, can keep the wound environment moist, allows gas exchange, protects the wound from microbial damage, and absorbs wound exudates. [10]

ANTI-DIABETIC DRUGS

Decreased insulin action is a hallmark of diabetes. Systemic insulin treatment is used for glycemic control and according to the CDC, over 6 million Americans use insulin as daily diabetes treatment. [11]

GROWTH FACTORS

Growth factors are naturally occurring polypeptides involved in cell growth, proliferation, migration, and differentiation. [12]

STEM CELL THERAPY

There are thousands of cells undergoing constant daily dynamic changes, such as self-renewal, to maintain tissue homeostasis. [13] Self-renewal is mainly driven by stem cells. [14]

NANOTECHNOLOGY

There is wide range of applications of nanotechnology in the field of drug delivery and furthermore, to simplify the oral absorption of proteins and peptides nano carriers are modified with specific ligands. [15] Nanotechnology in diabetes research has facilitated the development of novel glucose measurement and insulin delivery modalities which hold the potential to dramatically improve the quality of their life for diabetes. It is being used to improve the ease, efficacy and safety of insulin replacement therapy. Insulin delivering

nanoparticle technology is rapidly maturing and some early generations are in the clinic. Nanotechnologies recently reported for wound healing include:

- Nanomaterials
- Silver nano materials
- Copper nanoparticles
- Zinc oxide nanoparticles
- Carbon-based nanoparticles
- Gold nanoparticles
- Scaffolds
- Gene therapy
- Growth factor therapy
- Stem cell therapy
- Nitric oxide nanoparticles etc…,

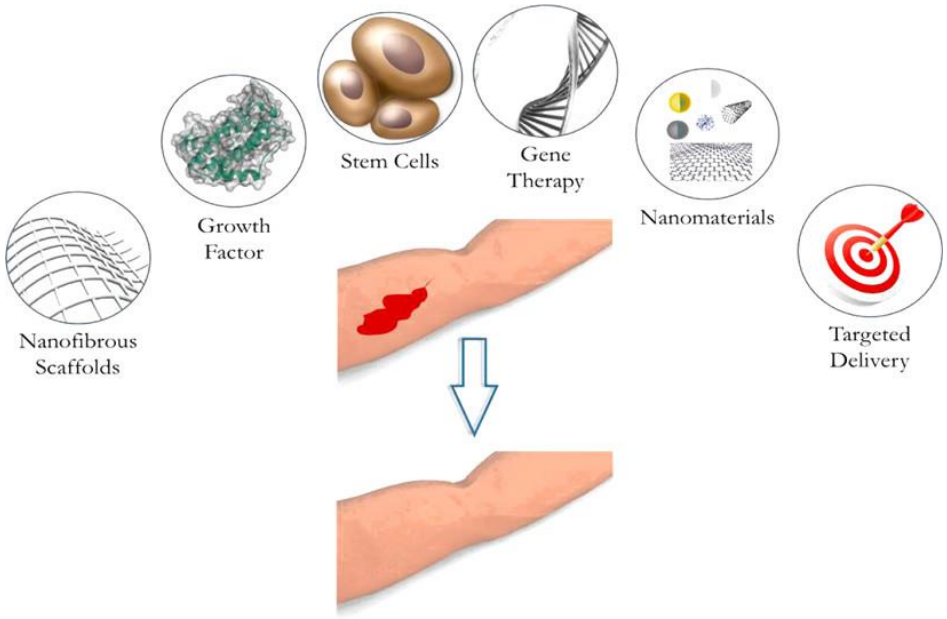


Fig 9: Different types of nanotechnology used for wound healing

An increasing number of innovative therapies have emerged in the field of wound healing and are currently under clinical investigations. There are 2 main categories of nanomaterials used in wound healing:

1) Nanomaterials that exhibit intrinsic properties beneficial for wound healing.
2) Nanomaterials employed as delivery vehicles for therapeutic agents.

Nano materials as intrinsic therapeutic agents include:

- Metallic and metal oxide nano materials
- Non-metallic nanomaterials

Nano structures as Carriers for Therapeutic Agents:

- Nitric oxide containing Nano carriers
- Antibiotics and antioxidants containing Nano particles.

CONCLUSION

Diabetic foot ulcer is a leading cause of amputations, affecting 15% of the people with diabetes. Chronic wounds often occur in patients with diabetes mellitus due to impairment of wound healing. Uncontrolled diabetes may also affect circulation, causing blood to move slowly, which makes it more difficult for the body to deliver nutrients to wounds. Wound management in diabetic patients is of an extreme clinical and social concern. The hyperglycaemic environment promotes the formation of bio films and makes diabetic wounds difficult to treat. In treating diabetic wounds nanotechnology is involved.

REFERENCES

1. Taniguchi N, Arakawa C, Kobayashi T. On the basic concept of nanotechnology. In: Proceedings of the international conference on production engineering; Tokyo, Japan; August 26-29 1974.
2. National diabetes information clearinghouse.
3. International Diabetes Federation IDF Diabetes Atlas. Global estimates for the prevalence of diabetes for 2019, 2030 and 2045. 9th ed; 2019.
4. Lee N, Hyeon T. Designed synthesis of uniformly sized iron oxide nanoparticles for efficient magnetic resonance imaging contrast agents. Chem Soc Rev. 2012;41(7):2575-89. doi: 10.1039/c1cs15248c, PMID 22138852.
5. Torres-Torres C, López-Suárez A, Can-Uc B, Rangel-Rojo R, Tamayo-Rivera L, Oliver A. Collective optical Kerr effect exhibited by an integrated configuration of silicon quantum dots and gold nanoparticles embedded in ion-implanted silica. Nanotechnology. July 24 2015;26(29):295701. doi: 10.1088/0957-4484/26/29/295701, PMID 26135968. Bibcode. Nanotech. 26C5701T; 2015.
6. Butler JM, Dressman JB. The developability classification system: application of biopharmaceutics concepts to formulation development. J Pharm Sci. 2010;99(12):4940-54. doi: 10.1002/jps.22217, PMID 20821390.

7. Allen TM, Cullis PR. Drug delivery systems: entering the mainstream. Science. 2004;303(5665):1818-22. doi: 10.1126/science.1095833, PMID 15031496.
8. Mathieu D, Linke J-C, Wattel F. Non-healing wounds. In: Mathieu DE, editor. Handbook on hyperbaric medicine. Netherlands: Springer; 2006. p. 401-27. Menke NB, Ward KR, Witten TM, Bonchev DG, Diegelmann RF. Impaired wound healing. Clin Dermatol. 2007;25(1):19-25. doi: 10.1016/j.clindermatol.2006.12.005, PMID 17276197.
9. Enoch Sprice, P. 2004. Cellular, molecular and biochemical differences in the pathophysiology of healing between acute wounds, chronic wounds and wounds in the elderly. Archived 2017-07-06 at wayback machine.
10. Zuo N, Liwei G, Dong F, Wang S, Dang Y, Qing D. Research progress of electrospun nanofiber membrane based on chitosan for wound dressing. Chin Pharm J. 2019;54(14):1126-31.
11. Centers for Disease Control and Prevention. National diabetes statistics report: estimates of diabetes and its burden in the United States, 2014 [cited Jul 1 2015]. Available from: http://www.cdc.gov/diabetes/pubs/statsreport14/national-diabetes-report-web.pdf; 2014.
12. Barrientos S, Stojadinovic O, Golinko MS, Brem H, Tomic-Canic M. Growth factors and cytokines in wound healing. Wound Repair Regen. 2008;16(5):585-601. doi: 10.1111/j.1524-475X.2008.00410.x, PMID 19128254.
13. Hsu YC, Pasolli HA, Fuchs E. Dynamics between stem cells, niche, and progeny in the hair follicle. Cell. 2011;144(1):92-105. doi: 10.1016/j.cell.2010.11.049, PMID 21215372.
14. Cosgrove BD, Gilbert PM, Porpiglia E, Mourkioti F, Lee SP, Corbel SY, et al. Rejuvenation of the muscle stem cell population restores strength to injured aged muscles. Nat Med. 2014;20(3):255-64. doi: 10.1038/nm.3464, PMID 24531378.
15. Veiseh O, Tang BC, Whitehead KA, Anderson DG, Langer R. Managing diabetes with nanomedicine: challenges and opportunities. Nat Rev Drug Discov. 2015;14(1):45-57. doi: 10.1038/nrd4477, PMID 25430866.