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Review Article

Nanotechnology in Identification and Controlling of Diabetic Retinopathy: An Outlook

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Abstract
Diabetic retinopathy is a complication in diabetes which affects the eyes by damaging the blood vessels of retina. The nanotechnology enhances the bioavailability and permeability of drug in the retina as it can help to cross the barriers of eye like cornea, conjunctiva and blood retinal barriers (BRBs). Nanotechnology ("nanotech") is manipulation of matter on an atomic, molecular, and supramolecular scale. It is consequently conjoint to see the plural form "nanotechnologies" as well as "Nano scale technologies" to rise to the expansive assortment of research and solicitations whose conjoint peculiarity is size. Because of the variability of potential capitulations (containing industrial and military), executives have endowed billions of dough in nanotechnology exploration.

Keywords: *Nanofibers, electrospining, electrostatic forces, drug-polymer interactions, posterior anatomy of eye, dosing frequencies.*

Introduction

Diabetic retinopathy, the leading cause of blindness, is characterized by early retinal microvascular dysfunction. Endothelial damage is linked to increased leukocyte adhesion and leads to blood-retinal barrier breakdown and diabetic macular edema, the main cause of vision loss in diabetes. When the sugar level rises in the blood it can cause damage by swelling and leakage of blood vessels of retina. In some cases, these vessels will swell up (macular oedema) and leak fluid into the rear of the eye. In other cases, abnormal blood vessels will grow on the surface of the retina. Unless treated, diabetic retinopathy can gradually become more serious and progress from 'background retinopathy' to seriously affecting vision and can lead to blindness.

Mechanism of Diabetic Retinopathy

Over time, high sugar glucose levels can weaken and damage the small blood vessels within the retina. The hyperglycemia causes oxidative stress, inflammation and activation of other pathways which increases the level of cytokines and VEGF in that area. Increased level of VEGF causes neural dysfunction and increased vascular permeability leading to DR and ultimately vision loss. The whole process is briefly shown in fig.1.

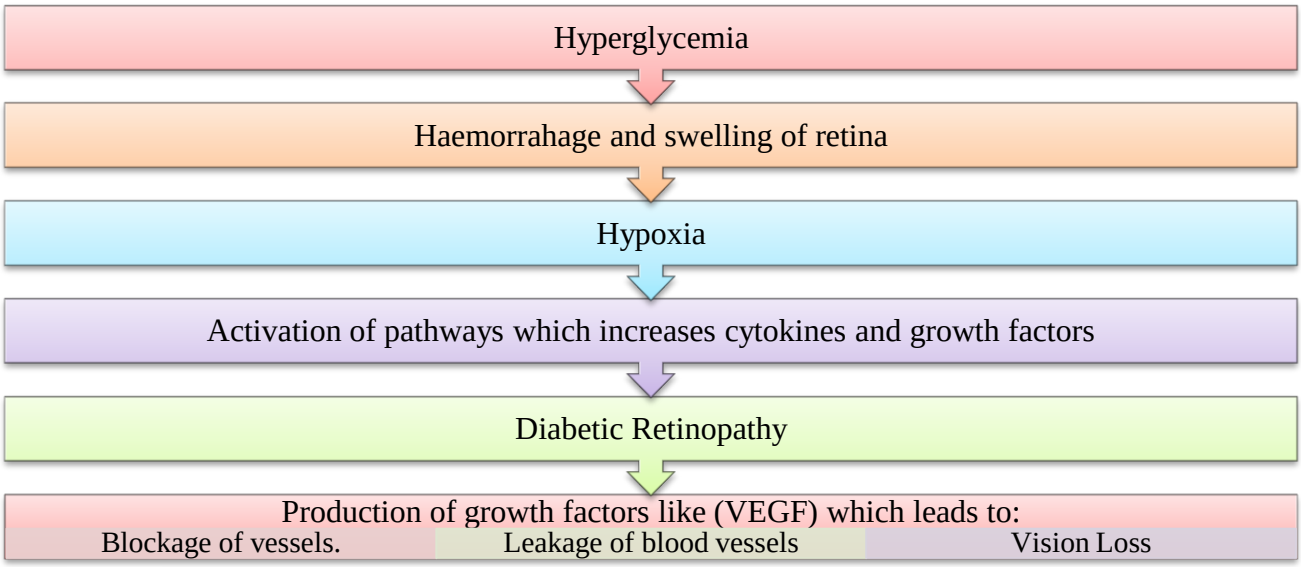

Fig. 1: mechanism of diabetic retinopathy

Symptoms

The early stages of diabetic retinopathy may occur without symptoms and without pain. An actual influence on the vision will not occur until the disease advances. Macular oedema can result from maculopathy and affect vision occurs if leaking fluid causes the macular to swell. New vessels on the retina can prompt bleeding, which can also block vision in some cases. Fig. 2 depicts some symptoms of DR.

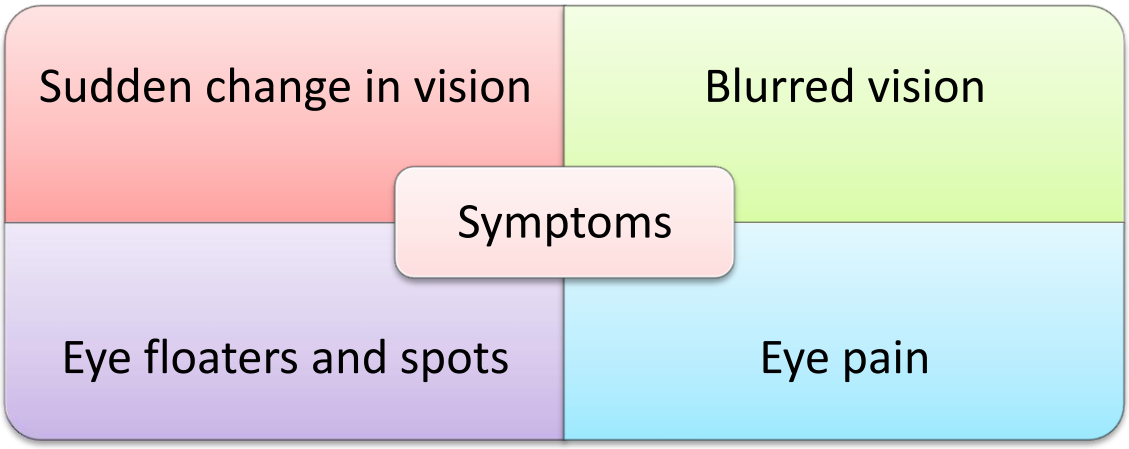

Fig. 2: symptoms of DR

Risk factors for diabetic retinopathy include

- **Diabetes.** The population of type 1 and type 2 diabetes remains the revenues of hazard in place of undeveloped diabetic retinopathy. [13] Increased level of diabetes lead to the increased risk of diabetic retinopathy.
- **Race.** Hispanics and African Americans exist by the side of imposing hazard in lieu of growing diabetic retinopathy.
- **Medical circumstances.** Societies using supplementary curative circumstances,[14] such as in elevation of body fluid compression plus in elevation in cholesterol remain by the side of inordinate danger.
- **Pregnancy** Pregnant womanhood expression a sophisticated possibility in lieu of unindustrialized diabetes and thus diabetic retinopathy. Female progressing with gestational diabetes is also prone to retinopathy.

Treatment of diabetic retinopathy: Diabetic retinopathy can be prevented by proper diabetes management and regular checkups. Mild cases of DR are easily curable but in case of advanced DR laser treatments and surgical procedures are required. The treatment involves virectomy, laser surgery, medical control and medication.

1. Vitrectomy: Surgical treatment for diabetic retinopathy is removal of the vitreous gel (vitrectomy). Vitrectomy does not cure the disease but it may improve vision in people who have developed bleeding into the vitreous gel (vitreous hemorrhage), retinal detachment, or severe scar tissue formation.

2. Laser surgery: Laser photocoagulation uses the heat from a laser to seal or destroy abnormal, leaking blood vessels in the retina.

3. Medical control: Proper diet and regular checkups can control the blood sugar level and thus can prevent vision loss and keeps the blood vessel of eyes healthy.

4. Medicines: One type of medication is called "anti-VEGF" medication. This helps to reduce swelling of the macula, slowing vision loss and perhaps improving vision. This drug is given by injections (shots) in the eye.

Unfortunately the available treatments are not able to treat the condition due to many reasons. Some of the reasons are discussed in the table 1.

Table 1: advantages and limitations of the treatments available for DR

Treatment	Disadvantages
Vitrectomy	It becomes too late for vitrectomy in many cases and also the vision may decline even after the procedure
Laser surgery	Costly and uncomfortable for patient as a very bright light is flashed in the patient's eye
Medical control	Not effective specially in case where the DR is already residing
Medicines	Painful and patient incompliance occur as injections and shots have to be taken

Nano technological approaches

The earliest and widespread definition of nanotechnology referred as a technology with objective of fabricating molecules of size range in nanometers and thus also referred to as molecular nanotechnology. Because of the variety of potential applications (including industrial and military), governments have invested billions of dollars in nanotechnology research. Until 2012, through its National Nanotechnology Initiative:

- the USA has invested $3.7 billion,
- the European Union has invested $1.2 billion and
- Japan has invested $750 million

Some of the nano technological systems used in treatment of diabetic retinopathy are discussed in table 2.

Table 2 comparison of different delivery systems

Carriers	Size	Possible route of administration	Advantages	Limitations
Liposomes	50-100 nm	Oral, topical and parenteral	Both hydrophilic and lipophilic drug can be loaded, can stay longer in targeted tissue	Costly and leakage of loaded drug may occur
Nanogels	20- 200 nm	Topical and subcutaneous	Biocompatible and biodegradable, controlled delivery	Costly and remaining surfactant may cause toxicity
Dendrimers	<10 nm	Oral, topical and parenteral	Can be carry both hydrophobic or hydrophilic drug and increased absorption	Interact with biological membranes leading to destabilization and cell lysis
Carbon nanotubes	1-100 nm	Oral, topical and parenteral	High drug loading efficiency, targeted delivery	Toxic and can accumulate in tissues
Nanofibres	1-100nm	Oral, topical and parenteral	High drug loading, targeted delivery, sustained release	Residual solvents can be toxic

Liposomes

Liposomes are artificial spherical vesicles which are formulated by cholesterol and nontoxic phospholipids. They are very small in size and can load both hydrophilic and lipophilic drugs as they have an aqueous core and a phospholipid bi layer. They have gained interest in field of drug delivery as they resemble to the biological membrane due to the phospholipid bi layer.

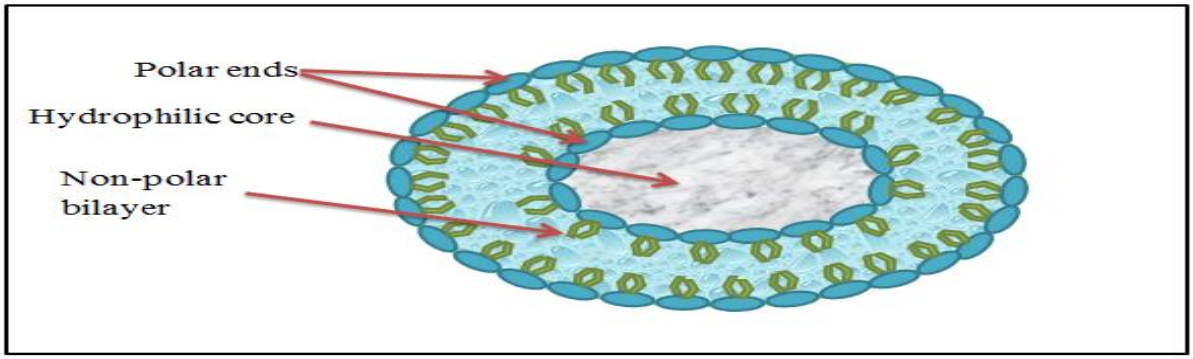

Fig. 3: liposome

Nano gels

Nano gels at present are extremely inflamed as they can integrate approximately 30% wt. of drugs then consequently can diminution their attentiveness through 30 folds, deprived of snowballing the poisonousness of the drug. They offer properties like confrontation in contradiction of dilapidation, in elevating the drug loading besides the probability of transport mechanical remainders superficial to peripheral motivations, such by way of pH, infection, light and redox reactions.[20]

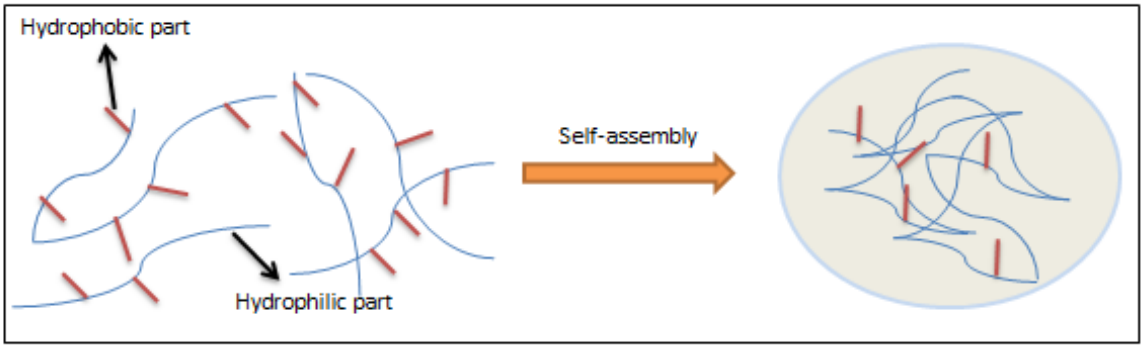

Fig.4: nano gels

Dendrimers

Dendrimers are Nano scale amalgams created through the uninterrupted accumulation of deposits of separating assemblages. The situation at present exceeding lypronged multifactorial plus presence of many chain terminals aimed to increase solubility, miscibility then intended for high reactivity.[21] The size and its capacity of directing ligands concentrates dendrites eye-catching aimed at procedure voguish drug delivery.[22]

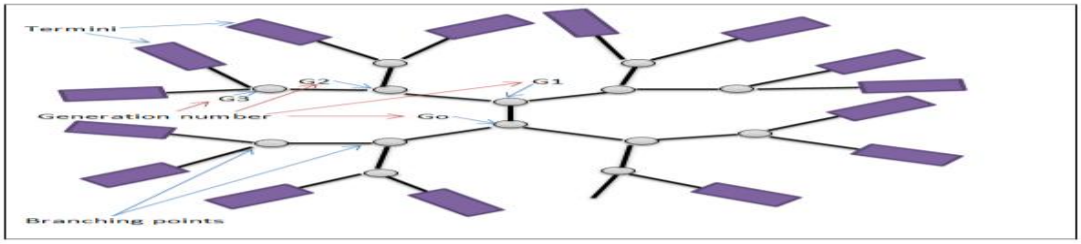

Fig.5: dendrimers

Carbon nano tubes

Carbon nano tubes (CNTs) are defined as allotropes of *carbon* through a cylinder-shaped nanostructure. *They* are situated tremendously small tubes with either a single or multi layered carbon construction which brand them an alluring contender toward summarize treatments confidential their fissures.

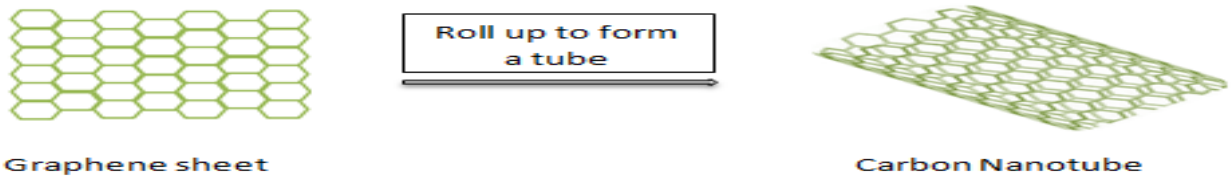

Fig. 6: nano tubes

Nano fibers

Nano fibers are fibers fabricated by electrospinning method which prepared fibers of diameter in nanometers and have different physical properties and application potentials.[2] The diameters of Nano fibers depend on the type of polymer and method used to fabricate them. The main objective of polymers and their fabrication as nano fibers is to achieve high capacity, high absorbency and high strength as compared to the microfibers.

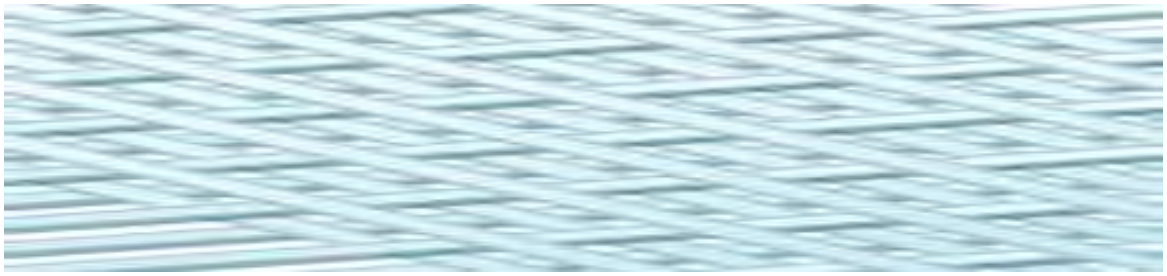

Fig. 7: nano fibers

Fabrication of Nano fibers

Nano fibers can be generated from different polymers and hence have different physical properties and application potentials. Many different methods exist to make nano fibers, including drawing, electrospinning, self-assembly, template synthesis, and thermal-induced phase separation. Electrospinning is the most commonly used method to generate nano fibers because of simple setup, cam produce continuous nano fibers and the diameter of nanofiner produced can be cotrolled.

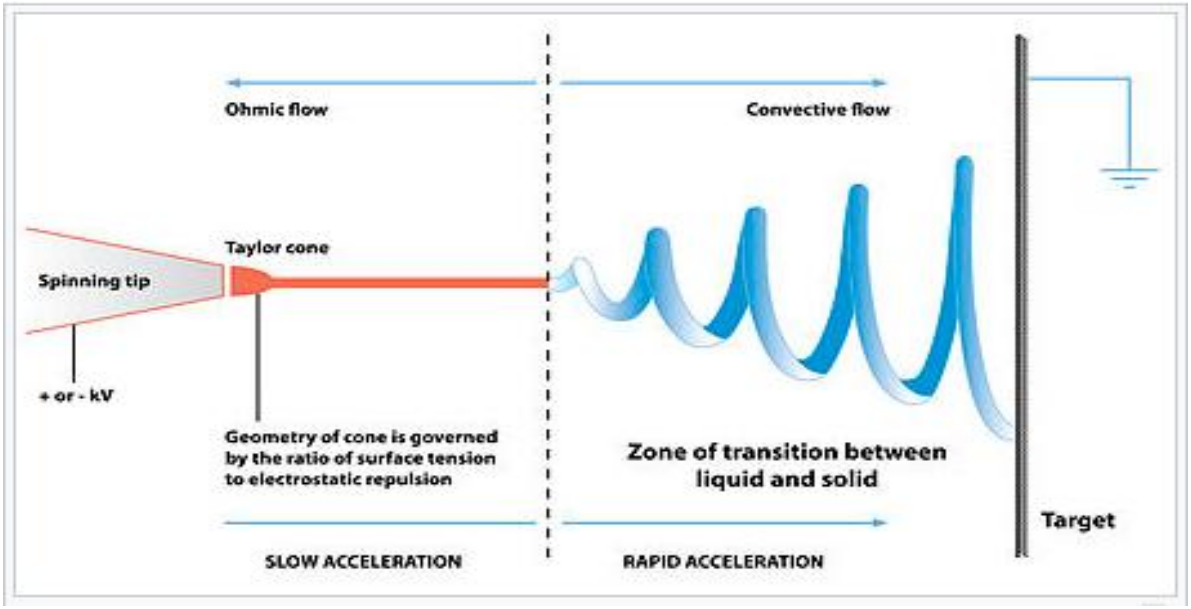

Fig. 8: electrospinning

Components of Electrospinning

The main components of the electrospinning process can be classified as:

(i) Syringe (or spinneret),

(ii) High voltage supply,

(iii) Collector.

Syringe: It contains the polymer solution and is connected with a electrode. Electric field is applied to the syringe which emits the polymer solution out of the needle. The diameter of needle is also an important parameter to be kept in mind at the time of electrospinning. The spinneret plays a very important role in the type of nanofibres produced.

High voltage supply: High voltage supply is a crucial parameter in fabrication of nanofiber. High voltage supply leads to formation of electric field and ejection of charged polymers from spinneret. This electric field helps in quick evaporation of solvent and stretching of polymer towards the collector.

Collector: The charged fibers are attracted towards the collector. Type of collector affects morphology of properties of nanofibers. Different type of collectors are used: Rotating drum collector, moving belt collector, rotating wheel with beveled edge, multifilament thread, parallel bars, simple mesh collector etc.

Parameters to be checked before electrospinning

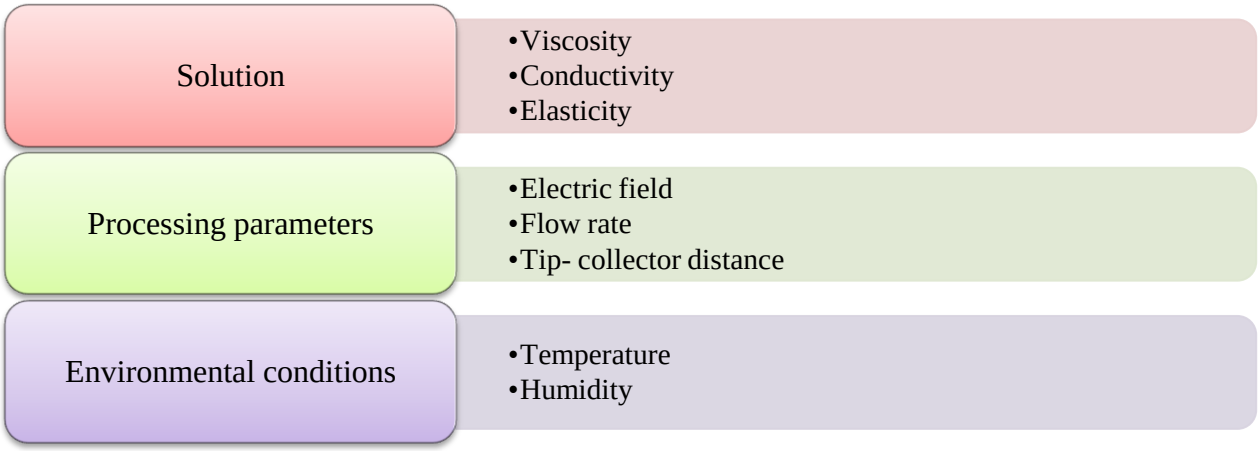

Fig. 9: parameters

Process involved in Electrospinning method

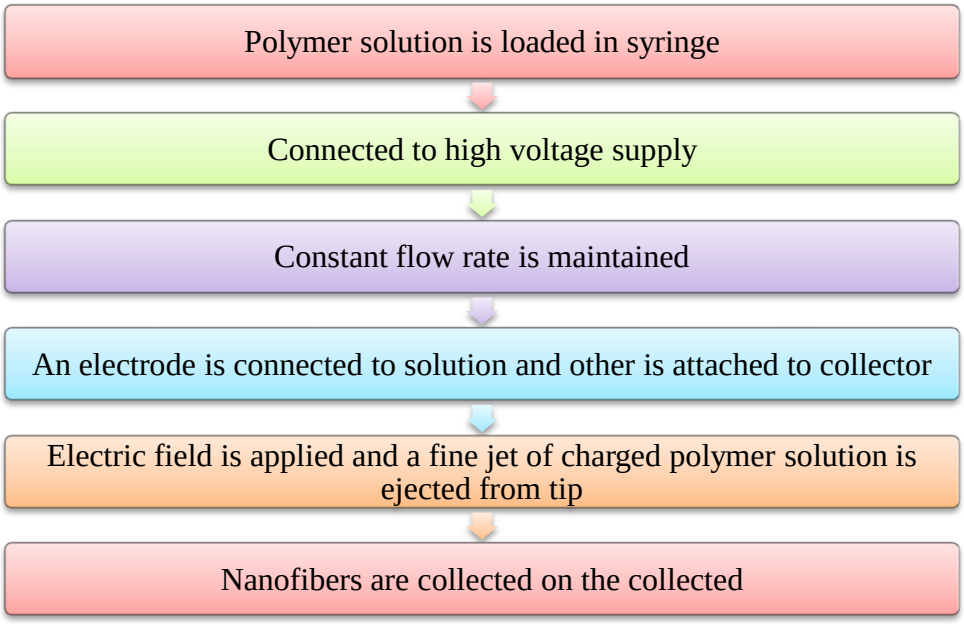

Fig. 10: process of electrospinning

Advantages

Nanofibers have emerged as a good carrier system in those cases where controlled delivery is required. due to its properties and advantages this system has gained interest in the diagnosis also. The researchers are focusing on futuristic aspects of nanofibers. Fig. 10 depicts some of the advantages of nanofibers.

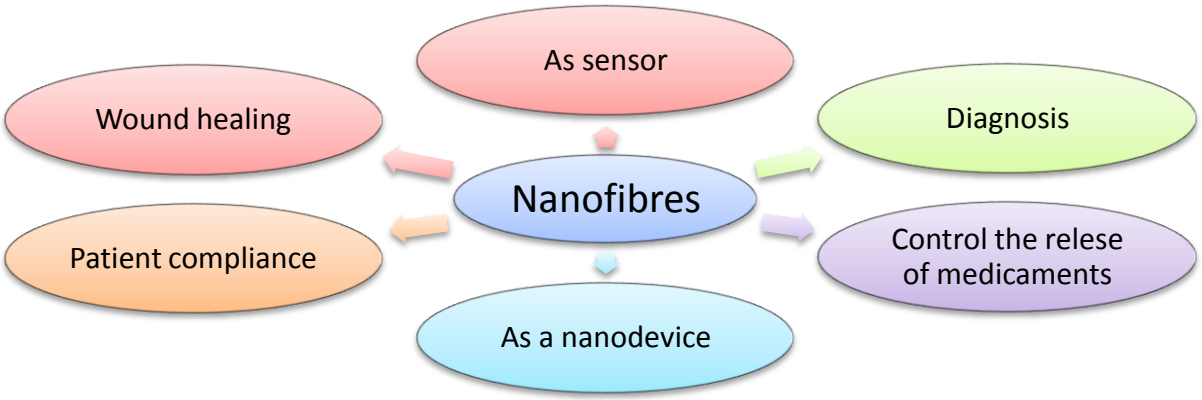

Fig. 11: advantages of nanofibers

Conclusion

The management of appropriate carrier system may transform the therapeutic efficacy of drugs. Nanoparticles are respectable carrier coordination for delivery of drugs but the foremost disadvantage of the nanoparticles is that the drug loading is inadequate and they can sabbatical the toxic metabolites in the body. The poisonousness of carriers is of concern when the toxic metabolites circulate in the blood stream and they get accumulated. The Excellency of the carrier system is important and it depends on the need of therapy, the drug and its physical properties. The carrier system should be nontoxic and should be biocompatible. They should target the site and should give prolonged activity to overcome the multiple dosing problems. There is a need of proper drug delivery systems that could maintain a steady release of drug to the specific site of action and to optimize the therapeutic properties of drug products and render them more safe, effective, and reliable. The nanofibers prepared from electrospinner have solved most of the problems associated with the frequent dosing and long term therapy of drug. The new advancements in the electrospinner have made it possible to fabricate nanofibers with good strength and efficacy. The advancements in drug delivery system are mainly objected on fulfilling the need of pharmaceutical industries and clinical importance.

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