EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 6
Issue: 3
178-182
Year: 2019

NEEDLE FREE INJECTION TECHNOLOGY

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Article Received on 23/12/2018 **Article Revised on 14/01/2019** **Article Accepted on 05/02/2019**

ABSTRACT
The Needle-free injection (NFI) systems are novel ways to introduce various medicines Needle free injection technology was developed to reduce the number of needle stick accidents and associated problems. It is an extremely broad concept which includes a wide range of drug delivery systems that drive drugs through the skin which propels the drug through the skin, virtually nullifying the use of hypodermic needle. Needle-free technology offers very obvious benefit of reducing patient's concern about the use of needle. Needle free injection gives effective injections for the wide range of drugs and bioequivalent to syringe and needle, results in less pain, and is strongly preferred by patients. This technology is not only thought to be beneficial for the pharma industry but developing world also and finds it highly useful in mass immunization programmes, bypassing the chances of needle stick injuries and avoiding other complications including those arising due to multiple use of single needle, also it has the added potential to increase compliance with dosage regimens and improved outcomes. Due to an ultrafine stream of high pressure fluid is created, that penetrates the skin devoid of the use of a needle, thus faster administration of drug occurs as compared to conventional needles. The main aim of modern needle-free drug delivery system is to enhance the prescribing and adoption of important drugs that require self-injection, such as biologics. Therefore, Needle free systems are designed to solve the problems created due to conventional needles making them safer, less expensive, and more suitable. In this review we aims to discuss about the needle less drug delivery system, their applications and advantages over needle injections. Today, they are many steadily developing technology that promises to make the administration of medicine more efficient and less painful.

KEYWORDS: Needle Free Injection Technology, Powder, Liquid, Depot Injection, Injector, Components.

INTRODUCTION
Needle free injection technology (NFIT) encompasses a wide variety of drug delivery systems that drive drugs through the skin using any of the following forces as Lorentz, shock waves, pressure by gas or electrophoresis which set in motion the drug through the skin, virtually nullifying the use of hypodermic needle.

The devices as such mentioned above are available in reusable forms. In contrast to the traditional syringes, NFIT not only gives the user freedom from unnecessary pain but also the drugs in the form of solid pallets can also be administered.

The major drawback associated with this technology is post administration "wetness" of the skin which , if not taken care of, harbor dust and other unwanted impurities. This technology is being backed by organizations such as World Health Organization, Centres for Disease Control and Prevention and various groups including Bill and Melinda Gates Foundation.

Additional benefits includes very fast injection when compared to conventional needles and no needle disposal issues. Not only it benefits the pharmaceutical industry in increasing product sales, it has the added potential to increase compliance with dosage regimens and improved outcomes. Today, they are a steadily developing technologies that promises to make the administration of medicine more efficient and less painful. To overcome the obstacles related to needle based injections, needle free injection technologies (NFIT) have gained popularity during the past few years and offer many benefits. These technologies are meant for injecting liquid formulations, as well as injecting drugs and vaccines in a solid particle dosage form. Needle free injection system is novel way to introduce various types of medicines into patient without piercing the skin with conventional needle. They can take the form of powder sprays, edible products, inhalers and skin patches.

Methodology
Needle-free technology, which was first called as jet injectors, were developed in the 1930s and used as mass

vaccination programs in people for smallpox, polio, and measles. Using mechanical compression to force fluid through a small orifice, these devices produced a high-pressure stream that could penetrate through the skin and subcutaneous tissue to deliver the vaccine. Most of the oldest devices used the same nozzle faces and fluid pathways to dose all the individuals; thereby causing potential safety hazards of transferring blood-borne pathogens between individuals.

The entire needleless devices operating by the same principle of creating a high pressure (>10MPa) jet of liquid (velocity 100m/sec) contains the drug that penetrates the skin. Through effective control of the pressure, the device can deliver the drug solution or suspension into the subcutaneous, sub dermal or intramuscular layer depending on the demanding application. In general needle free technology works by forcing liquid medication at high speed through a timing aperture that is held against the skin. This creates an ultrafine stream of high pressure fluid that penetrates the skin without use of needle.

Types of Methods

1. Powder injections.
2. Liquid injections.
3. Depot or Projectile Injection.

All these technologies have same basic principle of delivering medication by pressurized contact of fluids with skin.

Method Type 1-Powder Injection

Powder injections Design of powder injection systems: It consists of a chamber filled with solid drug content and a nozzle for firing drug particles into the skin by utilizing the power source which naturally is compressed gas. The injection has a diaphragm on either side of chamber to cover the drug chamber.

Method Type2 – Liquid Injection

The basic principle involved in this injection is "if a high enough pressure can be generated by a fluid in intimate contact with the skin, then the liquid will punch hole into the skin and delivered into the tissues in and under the skin." The same principle is applied as in powder, but there is a contrast in actual design and operation of the powder injection devices. These systems uses the gas or spring, pistons, drug loaded compartments and nozzles. Naturally, the nozzle has an orifice size of about 150 to 300 μm.

Mechanism of liquid injections

• Impact of a piston on liquid reservoir in the nozzle increases the pressure, which shoots the jet out of the nozzle at a high velocity greator than 100m/s.

• The effect of the jet on the skin surface starts by the formation of a hole in the skin through erosion, fracture, or some other skin failure mechanisms.

• Further the impingement of the jet increases the depth of the hole in skin. If the volumetric rate of hole formation is less than the volumetric rate of jet impinging the skin, then some of the liquid moves back towards the injector.

• The gathering of liquid in the hole occurs because of a deeper hole in skin which slows down the incoming jet. Hence, further development of a hole is ceased. The extent of the hole are established very early in the process from the time of impact. Stagnation of jet at the end of the hole disperses the liquid into the skin in a near-spherical shape.

Method Type 3- Depot (Or) Projectile Injection

These systems are plotted for administration of a drug into muscles. They create a store of drug into muscles that releases continuously over a desired period of time.
The drug is processed into a long thin depot having sufficient mechanical strength strong enough to transmit a driving force to a sharp tip which may be formed either from an inert material or medicament itself.

A depot is in the formed of the measuring cylinder around 1mm in diameter and few millimeters in length. This dimension may be small enough to limit the payload, but the quantity of the payload is sufficient enough for many new therapeutic proteins, antibodies, molecules. The depot is strong enough to pierce the skin when pierced with the sharp tipped piercer by applying a pressure of the 3-8 mega Pascal (MPa). For a depot preparation of around 1 mm, few Newton's of force are required. The transport device, therefore, would employ the transfer of energy from a suitable "spring".

On the Base on Site Of Delivery

Intradermal injector: These systems has been employed to deliver comparatively newer, DNA-based vaccines to the intradermal layer of skin. The system delivers the drug at a very shallow depth i.e ; between the layer of the skin.

Intramuscular injector

This is one of the most developed NFIT systems employed for the intramuscular drug administration. Drug delivery via this system is the deepest among all other systems.

Drug delivery through NFIT devices has been most successful as for the vaccination.

Subcutaneous injector: Certain therapeutic proteins including the human growth hormones has been administered by this system. The medicament is transported to the adipose layer just below the skin.

Table. 1. Medication Delivered Via Needle Free Injection.

Medication Delivered Via Needle Free Injection	
Drug	**Usage**
Vaccines	Immunization
Insulin	Blood Sugar Control
Growth Hormones	Increase Growth Rate
Lidocaine	Anesthetic
Midazolam	Sedative
Erythroprotein	Proteins for DNA Therapy
Interferon	
Botulinum Toxin	

Components of Needle–Free Injection

Needle-free injection devices consists of three main components.

Component 1 –Injection Device

It has a drug chamber and is plotted such that self administration is possible. The device is made up of plastic. Sterility is maintained throughout the device. It has a sterilized needle-free syringe which is also made of plastic.

Component 2- Nozzle

The nozzle serves as the passage for the drug and serves as the skin approaching surface. The nozzle has an perforation through which the drug enters skin when injected. The diameter of perforation is typically 100 μm. The nozzle shoots drug particles at a typical speed of 100 m/s with a depth of 2 mm. The most usual orifice size is 0.127mm, compared to a 25-guage needle. Therefore this injection is painless; the patient feels tap of gas on the skin which is like swish your finger against your skin.

Component 3-Pressure Source

It is important for transporting a drug forcefully into the systemic circulation through the skin. The pressure source can be mechanical method which stores the energy in a spring and is released by pushing a plunger to provide the necessary pressure. It can also be pressure storage method that utilizes compressed gas. The most popular gases which are used in devices are carbon dioxide or nitrogen. Pressurized metal air cartridges are usually provided for access in portable units. The accuracy of drug delivery and stress imposed on the product is influenced by device design. The device must assure the generation of sufficient high pressure to cause skin piercing as well as not harming the drug molecule. Brittle drug molecules are vulnerable to damage due to high pressure like monoclonal antibodies. Devices may vary in design which depend upon the drug for which they are used.

Mechanism

The mechanism generates force by using compressed gas to propel the drug through an orifice at a very high speed.

While administration of drug occurs through the device, an ultra-fine stream of fluid pierce through the skin layers which delivers the drug very quickly into the systemic circulation.

1. Peak pressure phase - optimal pressure required for penetrating the skin lasts about < 0.025 sec.
2. Dispersion phase - lasts about 0.2 sec.
3. The drop-off phase - lasts about < 0.05 sec.

Advances in Needle Free Injection Technology

1. Needle Free, auto and Pen Injector

An auto injector is a medical device designed to transport a single dose of a particular drug.

Most of the auto injectors are spring-loaded syringes. By design, autoinjectors are comfortable to use and are intended for self administration by patients, or administration by the untrained personnel.

The site of injection depends on the drug loaded, but it is usually administered into the thigh or the buttocks.
The injectors were firstly designed to overcome the hesitation associated with self administration of the needle-based drug delivery devices.

Advances in auto injector design and in needle free injectors are helping pharmaceutical companies to market their drugs and to compete more by introducing gains in market share, allowing greater penetrability of markets, helping patients to follow with dosage regimes and providing safer injections.

Indeed, injection devices were once considered as the afterthought but now in some product categories they are becoming an entry ticket, without which they would fail to attract patients.

Pharmaceutical companies are developing injectors in parallel with their new drugs, in the knowledge that a device will be needed at product start.

Auto injectors are advancing both commercially and technically with the recent inaugration of a second pre-filled single-use device, containing a standard pre-filled syringe, which automates needle insertion, drug delivery and automatically covers the needle after use.

In parallel to auto injector development there has been significant advances in needle-free and powder delivery which are increasingly showing that they offer an alternative to the needle.

2. Intraject Systems

Intraject system is the world's first disposable, needle free injection device for the delievery of liquid medicaments which were Invented by terry wetson.

Intraject is specially made to meet the patient needs; being pre-filled and disposable system is designed for unobtrusive, contamination free self-injection.

With minimum training a practioner, patient can deliver a reliable, virtually pain free injection.

It is replaced by pre-filled syringes and autoinjectors in many commercial product areas.

Intraject offers pharmaceutical companies the opportunity to extend the product lifestyle and manage patent expiry.

The system is designed for simple manufacture and, as a prefilled device, provision of pharmaceutical licencees with exclusivity which is critical for successful product differentiation at low cost.

3. Bioject®Zetajet

The Bioject®ZetaJet™, Bioject's latest advance in needle-free delivery systems, consists of two components, the portable injector and the autodisabling disposable syringe.

It is planned for the delivery of vaccines and injectable medications either subcutaneously or intramuscularly and is indicated for both professional use and for patients who self-inject.

The syringe assembly has a special "auto-disable" feature that prevents re-use of the syringe.

The Bioject®ZetaJet™ has FDA clearance for delivering the subcutaneous or intramuscular injections of liquid medication, including vaccines and other injected medications.

4. Injex Needle – Free Injections for Infiltration Anaesthesia: INJEX Pharma offers a solution for previous local anaesthesia problems, a needle-free injection system. The INJEX System uses an injection ampoule with a micro aperture of only ø 0.18 mm through which the anaesthetic is administered under dosed pressure to the submucosa – virtually painless and exactly where it is required.

5. Madajet XL Podiatry Needlefree Injector

Comfortable and easy to use and virtually painless compared to needles. gives instant local anesthesia or regional blocking for most podiatric procedures.

It Minimizes tissue trauma and facilitates suturing as there is no tissue distention around the injection site.

It Provides anesthesia for deep needle insertion. May be used along with anesthetics, sterioids and other medicaments.

It Has interchangeable Tips for easy sterilization between patients. Can be used by all age groups.

Consistent depth of penetration is 4- 5.5mm below the epithelium and makes wheal at the base of the injection which is of 5-6mm in diameter.

Compatible volume of 0.1cc per injection intradermally permits approximately 38 injections with single loading (to 4.0cc).

May be sterilized by autoclaving or by usual sterilization process - do not use dry heat.

Objective of Needle Free Injection

The main Objective of needleless injection is to avoid the risk and compliance involved in conventional method and to be used in diseases like diabetes, skin disease, allergy, asthma etc.

Moreover these are user friendly and provide a takeaway home option. The frequency and the number of the dose can be known through it by usage of stroke counter present in the device.

The Future Scope

Patient's want safest and best method of taking their medicines.

Additionally, with increasing competition, pharmaceutical companies need new ways of comparing their product and extending the patent life on proprietary drugs.

Many of the needle-free alternative technologies are in the development stage. Companies are still working on manufacturing devices that are safest and easiest to use. They are working on alternatives which can transport even more types of medicines. Inhalers are being developed as are nasal sprays, forced air injectors and patches.

In the future, other food products may be genetically enhanced to deliver vaccines and other drugs. These include bananas and tomatoes.

In fact, bananas are being looked as vehicles for a vaccine to protect against the Norwalk virus. Tomatoes protect against hepatitis B which are also being developed.

In addition to new delivery systems, scientists are all in search of methods for producing long lasting drugs that will minimize the number of needle injections.

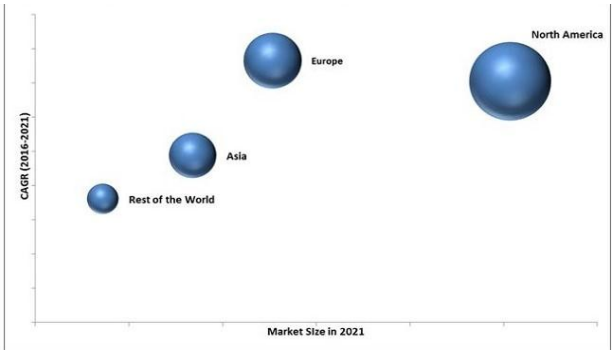

Figure. 1. Needle Free Injection Market System, By Region 2021.

Summary

Needle-free injection systems have potential to improve effectively. Major advantages of needle-free systems are the removal of broken needles, a more constant delivery of vaccines and drugs, and decreased worker safety risk. Needle free injection systems are customised to each operation and can be modified to optimize productivity. However, executing a needle free system can be challenging. Workers are require with skilled knowledge regarding any new technique. Initiation and training costs may also affect the interest in this technology for some pork producers.

CONCLUSION

Needle free technology offers very apparent advantage of minimizing patients fear regarding the use of needle. Other advantage comprises very fast injection as compared to traditional needles and needle disposal issues are rarely seen. Not only it assists the pharmaceutical industry in rising product sales, but also it has the extra tendency to increase conformity with dosage regimens and enhanced outcomes. In the developing world, there are foremost challenges of disease transmission due to reuse of needles which can be prevented by the use of Needle free injection technology.

These devices are suitable for delivery of drugs to some of the most sensitive parts of the body like cornea of eyes. They are efficient to administer in the intra-muscular, subcutaneous and intra-dermal injections. These systems require a energy source which may be obtained either physically or by the application of some force. The drug is forced ejected through a superfine nozzle.

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