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Review on Needle Free Injection System

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ABSTRACT

Needle free injection technology (NFIT)is an extremely broad concept which include a wide range of drug delivery systems that drive drugs through the skin using any of the forces as Lorentz, Shock waves, pressure by gas or electrophoresis which propels the drug through the skin, virtually nullifying the use of hypodermic needle. This technology is not only touted to be beneficial for the pharma industry but developing world too find 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. The NFIT devices can be classified based on their working, type of load, mechanism of drug delivery and site of delivery. To administer a stable, safe and an effective dose through NFIT, the sterility, shelf life and viscosity of drug are the main components which should be taken care of. Technically superior needle-free injection systems are able to administer highly viscous drug products which cannot be administered by traditional needle and syringe systems, further adding to the usefulness of the technology. NFIT devices can be manufactured in a variety of ways; however the widely employed procedure to manufacture it is by injection molding technique. There are many variants of this technology which are being marketed, such as Bioject® ZetaJetTM, Vitajet 3, Tev-Tropin® and so on. Larger investment has been made in developing this technology with several devices already being available in the market post FDA clearance and a great market worldwide.

Keywords:Immunization, syringe systems, needle stick injuries, propel, sterility

INTRODUCTION:

Needle-free injection techniques can be used to administer vaccines and medications in the pork industry. Needle-free injection offers a fast, effective route of administration. There are hazards that must be addressed to safeguard employees who utilize needle-free injection systems; therefore, an enforced education program is crucial to the success of using needle-free injection in any pork operation. Needle-free injection systems are novel ways to introduce various medicines into patients without piercing the skin witha conventional needle [1] .

The first hypodermic syringes were first developed by French surgeon, Charles Gabriel pravaz, in 1853, although there is a minor development in syringes since then, the technology has been remained unchanged for last 150 years. A needle-free system was first described by marshalllockhart in 1936 in his patent jet injection. Then in the early 1940's hyson and others developed high pressure "guns" using a fine jet of liquid to pierce the skin and deposit the drug in underlying tissue. These devices were used extensively to inoculate against infectious diseases and were later applied more generally in large scale vaccination program. Today, they are a steadily developing technology that promises to make the administration of medicine more efficient and less painful.

A. History[(2)]:

As long as drugs have been known to cure diseases, people have searched for better methods of delivering them. During the early nineteenth century researchers made a series of discoveries that eventually led to the development of the hypodermic needle by Alexander Wood in 1853. This device was used to give morphine to patients suffering from sleeping disorders. In subsequent years, the hypodermic needle underwent significant changes which made them more efficient to use, safer, and more reliable. However, needles still have significant drawbacks which prompted researchers to find needle-free alternatives. The first air-powered needle-free injection systems were developed during the 1940s and 1950s. These devices were gun-shaped and used propellant gases to force fluid medicines through the skin. Over the years, the devices have been modified to improve the amount and types of medicines delivered, and the efficiency and the ease of use.

B. Advantages of needle-free injection devices (NFID)[(3)]:

1. Safety:

Employees are less likely to be pricked with contaminated needles that can infect themselves with blood borne pathogens from accidental needle sticks. Furthermore, this system will eliminate the high numbers of tissue damage that results from when a needle breaks upon insertion into a patient.

2. Sterility:

Needle-free injections eliminate the possibly of reusing needles from one patient to another by eliminating the needle component all together. According to the World Health Organization, it is estimated that 40-70% of needle are reused and can cause patients to be infected with hepatitis, HIV, and other diseases. This technology will significantly decrease the spread of diseases and cross contamination.

3. Convenience :

For patients who need daily injections of medications, they no longer need to inject themselves with painful needles, but rather a simple and efficient needle-free injection that can be self-administered, require no prior training, and take less than 0.5 seconds.

4. Reduces costs :

This system will reduce the need of sharps disposal services and manufacturing of needles for injection.

5. Promotes patient compliance :

It is estimated that 10% of Americans are aichmophobia, belonephobia, or enetophobia; people who have a fear of sharp things, such as needles. With needle-free injection systems, it will enable patients to be more compliant on their medications and treatment plans.

6. Greater medication dispersion :

When using a traditional needle-based delivery system, the medication is delivered from the syringe as a spherical pool with the needle doing the penetration. However, the medication itself is responsible for penetrating the skin using needle-free injection systems and thus follows the path of least resistance. This results in a wider dispersion of the medication. This can provide greater efficacy.

7. Elimination of broken needles.

8. Consistent vaccine delivery.

C. Disadvantages of needle-free injection devices (NFID)[(4)]:

1. Higher start-up costs
2. Infrastructure for exhaustible gas systems
3. Higher requirement for training and maintenance
4. No one size fits all NFID
5. Worker confidence in NFID
6. Unreliable injection amount when using small volumes.
7. Often painful for patients.

Figure: 0.5ml Needle-Free Injector

I. TYPES OF NEEDLE FREE INJECTION SYSTEMS[5]:

Needle free technologies are of eight types:

A. Powder injections.
B. Liquid injections.
C. Depot or projectile injection.
D. Sonophoresis.
E. Micro needles.
F. Iontophoresis.
G. Electroporation.
H. Microporation.

All these technologies have the same basic principle of delivering medication by pressurizedcontact of fluids with the skin.

A) Powder injections:

The Powder injection system for particle delivery is the combination of a device with a specially formulated powdered drug. Unique devices have been configured for injection into any physically accessible tissue; nor-mal skin or mucosal sites. Some systems have been designed for single use and are completely disposable and others, intended for longer courses of therapy, have some reusable elements. For convenience and economy, reusable systems have only the drug and pressurized helium energy source in a single cartridge that is replaced for each injection.

The principle of all the devices is the same; i.e. the harnessing of the energy of a transient gas jet to accelerate a pre measured dose of particulate drug formulation. The most common orifice size is 0.127mm, com-pared to a 25-gauge needle, which is about 1mm. So, process is completely painless, "people feel the tap of the gas on the skin, it's like flicking your finger against your skin." So, device configuration will satisfy many therapeutic applications.

The Powder injection systems are powered by a manufactured helium gas aluminum micro-cylinder of ampoule design and use a drug cassette or package to introduce the powder into the gas flow. In operation, the micro-cylinder tip can be broken when the device is pressed against the tissue site to be treated .This releases the compressed helium suddenly to open the drug cassette for delivery of its payload to the tissue. The gas does not actually penetrate the skin, instead, it is reflected back in to the device through a silencer. The silencer is necessary because the flow is transiently supersonic. The other components of the device are manufactured from medical grade plastics using standard injection molding techniques.

B) Liquid injections:

The basic principle of this injection is "If a high enough pressure can be generated by a fluid in intimate con-tact with the skin, and then the liquid will punch a hole in to the skin and be delivered in to the tissues in and under the skin."

Although the same principle is applied as in powder but there is difference in the actual design and operation of the powder injection devices.Liquid jet injections use a high speed jet to puncture the skin and deliver drugs without a use of a needle. It can deliver macromolecules, vaccines, and small molecules. They must be capable of generating sufficiently high pressures that will force an ultra-fine jet stream of liquid medication into the patient's skin to deliver an appropriate dose. Typically, this is accomplished through the use of metal springs or compressed gas. The types of gases employed are carbon dioxide, helium, or nitrogen; however, spring loaded is preferred. Even though these devices are costly, they are very safe due to new needle stick injury laws. The device consists of a disposable needle-free syringe with a small orifice, commonly 0.127 nm, at the tip that fits within an injection device and when triggered delivers a quick burst of medication by puncturing the skin through erosion, fracture, or other skin-failure modes. These systems can administer subcutaneous injections delivered to the adipose layer just below the surface of the skin or intramuscular injections delivered into muscle tissue. Vaccines are typically given as intramuscular injections and therapeutic proteins are given as subcutaneous injections. Intradermal injections, which deposit medication between the layers of the skin, are in clinical trials. Intradermal injections are commonly used to deliver DNA-based vaccines and therapeutics.

C) Depot injections:

Depot injections are given in the muscle, where they create a store of a drug that is released continuously over a specified period of

time.

D) Sonophoresis:

Sonophoresis is a process that increases the absorption of topical compounds by transdermal delivery. It uses ultrasound-mediated skin permeation technology to deliver drugs through the stratum corneum. A low level of ultrasound energy, between 22-500 kHz, for less than 15 seconds is enough energy to cause transient disruption of the stratum corneum. Small drugs, such as hydrocortisone, as well as larger proteins, like insulin and erythropoietin, can be delivered through the stratum corneum using ultrasound technology. Cavitation is the mechanism of action that disrupts the stratum corneum; cavitations causes ubbles to form as a result of the ultrasound, causing transient disruption of the stratum corneum. Ultrasound is effective, as seen by determining blood glucose levels after transdermal delivery of insulin. With topical application of insulin, there is no chance for the insulin to diffuse through the thick layers of the skin, but by applying sonophoresis, you can get enough insulin through the skin into the systemic circulationto reduce blood glucose levels therapeutically.

E) Micro needles:

Micro needle patches have been used to deliver a wide variety of different low molecular weight drugs, biotherapeutics, peptides, proteins, hormones, skin repair agents, and vaccines. The patch is a 3mm x 3mm array that contains about 400 needles. The drug to be delivered can be on the surface of the polymer needle, integrated within the biocompatible and biodegradable needle, or both. These micro needles are between 20- 30 microns long, which is just long enough to penetrate the stratum corneum and deposit into the early part of the epidermis. However, because it is not long enough to extend into the dermis where the nerve endings are, no pain is felt with micro needles. Flux increases up to 100,000 times more than when a patch is applied to the skin.

With this new technology, the Nanojectcompany has designed a micro-needle delivery system that allows the injection of drug substances along with the ability to extract interstitial fluid for diagnostic purposes. One reason why they are able to do so is through their needle side holes. Positioning the holes at the side of the needle prevents coring leaving the channel open for delivery of medications or extraction of fluids.

As mentioned above, the micro needles are biocompatible and biodegradable. However, this was not always the case. Micro needles were first composed of silicon. This posed a problem due to the brittle nature of silicon causing 5% of the micro needles to break and remain in the skin and leading to drug loss, toxicity, and infection. To overcome this problem, micro needles are being formulated from metal and plastic, as well as biodegradable substances like maltose.

Advantages of Micro needles:

1. People will limit medical training can administer these devices in the form of vaccines topromote immunization programs.
2. The small micro needles provide highly targeted drug administration to individual cells.
3. Because the micro needles are so small, thousands are able to be fabricated on one patch leading to high accuracy and good reproducibility.
4. Micro needles store drug in a micro volume that is easily controlled and thus are capable ofaccurate dosing and enhanced stability.
5. Hollow micro needles can be used to remove fluid from the body for analysis as well as deliver micron volumes of medicinal liquid such as vaccines and insulin.

Disadvantages of Micro needles:

1. Expensive to manufacture and package.

F) Iontophoresis:

Iontophoresis delivers positively or negatively charged molecules (with some aqueous solubility) using an applied electrical field. It utilizes a small electrical current to drive drugs of opposite charge into the skin because of the electrical repulsion from the anode or cathode. The anode is the positively charged terminal that will repel positively charged molecules, whereas the cathode is the negatively charged terminal that will repel negatively charged molecules into the skin.

In the process of reverse iontophoresis, when an electric current is applied, it will drive drugs away from the cathode or anode depending on the drug properties, and it will draw sodium or chloride ions from the skin to the oppositely charged terminal. The buildup of sodium or chloride ions at the corresponding terminal causes an osmotic gradient and liquid from the skin (i.e. water) will diffuse to offset osmotic pressure differences. The detector can sample biofluid to detect an analyte of interest. This biological fluid can be sampled, as in glucose watches, to sample glucose levels in patients who have diabetes.

Ionsys was the first transdermal iontophoretic device. It was first marketed in Europe in 2006. It is a topical product that delivers fantail using an iontophoretic device. Compared to intravenous injection, topically applied fentanyl is able to achieve similar circulating blood levels (or greater depending on dose or extent of electrical current applied). Unlike the fentanyl patch which achieves maximum concentration at 24 hours, patient can achieve relevant concentrations of fentanyl in the blood quickly using iontophoresis.

G) lectroporation:

Electroporation involves applying an electrical field to increase permeability. This process uses high voltage, short duration pulses to produce aqueous pathways (holes) in the lipid membrane bilayers. This increases the flux through the stratum corneum (by 10,000-fold) for molecules that would not normally be able to pass through this layer, such as plasmid DNA. After pulsing, the cell membrane reseals within a few hours or days and the skin can heal so pores cannot be seen anymore. Therefore, electroporation is a transient, reversible process. It is being studied in late stage clinical trials for treatment of several cancersand vaccines for infectious diseases.

H) Microporation:

Microporation is a non-invasive transdermal delivery system of drugs and macromolecules. It combines a thin array of filaments with a patch containing the drug. Energy is pulsed and heat is producedby an electromagnetic field that burns small, transient pores into the stratum corneum to result in pathways for the diffusion of drugs. Clinical trials have shown this therapy achieves therapeutic concentration of drugs delivered in relatively shorter times.

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