International Journal of Research in Pharmacy and Allied Science (IJRPAS)
Published by Ideal Publication
Available at https://idealpublication.in/ijrpas/

A Detailed Review On Needle Free Injection Technology

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Article History

Received: 08/06/2023
Accepted: 03/06/2023
Published: 01/07/2023

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Abstract:
Needle free injection technology (NFIT) is an Innovative methods for administering a variety of medications to patients without puncturing their skin like conventional needle. These devices function by forcing liquid medication via a tiny aperture that is pressed up against the skin at a high rate of speed. This result in the creation of an ultrafine stream of high pressure fluid that enters the skin without the use of a needle, allowing the medicine to be administered more quickly than with conventional needles. Needle free injection technology are more advantageous than conventional needle and designed to solve problem associated with conventional needle. This devices is safe ,less expensive, also reduced needle phobia, self-administration is possible. Drug enter through the skin with high pressure without piercing the skin thus faster administration of drug is possible as compared to conventional needle. A number of different drug such as macromolecules like monoclonal antibodies, hormones, nucleic acid and vaccine can be administered using this techniques. Drug administered to the skin subcutaneous tissue, intramuscular tissue with very faster rate (upto 0.5 sec). This technology not only beneficial for pharmaceutical industry in increasing product but also increase patient compliance with dosage regimen and improved outcomes. Today they are a rapidly evolving technology that promise to improve the effectiveness and reduce the discomfort of administering drugs.

Keywords: Needle free injection, drug administration and Drug delivery, projectile injection.

INTRODUCTION.

Since 1937, jet injectors have been used to quickly provide vaccines to millions of people who need them. The Centre for Disease Control reported no more smallpox epidemics by 1990, demonstrating that the findings were credible.[1] Humans have had access to needle-free injection devices (NFID) since the 1930s. Because needle-syringe injection is inexpensive and simple to use, their adoption in farm production systems has been delayed. For protection against cholera, typhoid, tetanus, influenza, and other diseases, people receive shots. A needle's vaccination (or medicine) delivers systemic immunity when it is inserted through the skin. This is because the vaccination causes the body to produce antibodies that travel throughout the body when injected into the bloodstream. This techniques developed by Bioject Inc., the IjectTM needle-free injection device makes injecting drugs easy, comfortable, and safe. The system is affordable, pre-filled, simple to use, and completely needle-free.[2]

The aim of this review is to evaluating and summarizing needle free technology, its uses, mechanism of action and its stages of drug delivery.

The term "needle free" is used to describe a wide variety of drug delivery techniques, including those that use electrophoresis rather than a needle to deliver medications. Needle-free injection (NFI) devices are used for administering different medications to patients without puncturing their skin with a traditional needle. Needle free injection have many application such as it is used in field of inoculation and diabetes[3] and also showing positive impact on COVID 19.[4] During pandemics like those of influenza or COVID-19 vaccine shortages may occur due to the need for the vaccination of most people[5]. For better dispersion throughout a large tissue volume needle free injection needed. For both medical and non-medical aesthetic goals, needle-free injection can be utilized as well as Scars, wrinkles, condylomata acuminate, cutaneous tumors, persistent plantar warts, nail psoriasis, and hyperhidrosis are among the conditions that can be treated. Overall, needle-free injection is quite effective and secure, especially when carried out using gas-powered injectors; however, caution must be exercised when using high-pressure injectors in regions with relatively thin skin.

History

The first hypodermic syringes were invented in 1853 by French surgeon Charles Gabriel Pravaz; despite minor advancements in syringe technology since then, the technology has remained unchanged for the last 150 years. Marshall Lockhart's patent jet injection in 1936 was the first to describe needle-free drug delivery in the early twentieth century.

Then in the early1940s Higson and others developed high pressure “guns” using a fine jet of liquid to pierce the skin and deposit the drug in the 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 medicines more efficient and less painful.

Definition:

Needle free injection can be defined as a needle-free drug delivery method in which a high-speed stream of fluid impacts the skin and delivers a drug excluding vaccines and systemically absorbed medications like insulin. The fluid can contain a corticosteroid, an anaesthetic agent, on botulinum toxin A (BoNT-ONA), bleomycin, 5-aminolevulinic acid (ALA), or any injectable substance.

Advantages:

- Elimination of broken needles
- Consistent vaccine delivery
- Reduced vaccine volume
- Higher antigen dispersion
- Elimination of worker needle sticks
- Elimination of needle disposal
- Lower pain and stress.
- Patient compliance**.**
- Implementation of jet-injections for intradermal administration of medications makes the treatment almost pain-free and do not expose patients to long-term side effects [6].

Disadvantages:

- High start-up cost
- No one size-fits all system
- Greater complexity
- Cannot be used for Intravenous route
- Need for personnel training and maintenance [7]

COMPONENTS OF NEEDLE FREE INJECTION SYSTEM

Needle-free injection device consists of 3 main components :

Component 1- Injection device:

It is constructed with a drug chamber and is self-administration is attainable. Plastic makes up the device. The equipment is kept sterile at all times. It has a cleaned plastic syringe with no needles.

Component 2-Nozzle:

The medicine travels through the nozzle, which also acts as the skin-contact surface. The medicine is injected into the skin through an opening in the nozzle. Usually, the orifice's diameter is 100 m. Drug particles are released from the nozzle at a usual speed of 100 m/s and a depth of 2 mm. The most typical orifice size measures 0.127 mm, or about the size of a 25-gauge needle. As a result, the injection causes no pain; instead, the patient feels a tap of gas similar to when you flick your finger on your skin.

Component 3-Pressure source:

The medicine for injection receives its necessary driving energy from the energy source. Many of the products on the market store energy using mechanical or stored pressure components. In the mechanical approach, pressure is created by pushing a plunger, which releases energy stored in a spring. The pressure storage method uses compressed gas that is released during injection from a vessel.[8]

TYPES OF NEEDLE FREE TECHNOLOGY

1. Powder Injection

For skin delivery, the particles must only penetrate the skin's outermost barrier, the stratum corneum. As a result, drugs delivered reach the circulatory system faster than those administered subcutaneously.

All of the devices work on the same principle, the energy generated by a transient gas jet is used to accelerate a predetermined dose of particulate drug formulation. [9]

2 Liquid Injection

The fundamental idea behind this injection is that if a fluid is subjected to enough pressure, it will pierce the skin and will be injected into the skin's tissues, within, and underneath.

3. Depot or Projectile Injection

Depot injections are administered in the muscle, where they form a drug depot that releases continually for a certain amount of time. [10]

MANUFACTURING PROCESS

There are various methods of producing needle free injection system. The manufacturing process includes procedures like molding the component parts, putting them together, decorating, and labelling the finished item. To stop the transmission of illness, the entire production process is carried out in sterile conditions.

a. Molding the pieces:

This is the first step of manufacturing process. Here the plastic pellets are kept into a large holding bin on an injection molding machine. The pellets become flowable after attaining the required temperature; then the material is allowed to pass through the hydraulically controlled screw. It involves constructing the individual plastic components from plastic pellets

b. Assembling and labelling the pieces:

The next step is to put the pieces together and move them to an assembly line. Several things happen throughout this production process. These machines produce each printing, and because they have been specifically calibrated, each printing is extremely precise. The gadgets are put together either manually or with the aid of automation, depending on their complexity. This entails adding any buttons and installing the various components into the main casing.

c. Packaging :

The next step after the assembling process is packaging. The systems are packaged into cardboard boxes or plastic boxes after being wrapped with sterile films. Each component is packed to minimize movement, which helps to avoid damage. For consumer goods, an instruction manual is supplied, along with safety advice.

These cartons are then loaded onto pallets and transported to distributors by truck.

QUALITY CONTROL

Throughout the manufacturing process, line inspectors closely monitor the entire process to look for any cosmetic flaws or structural irregularities. Along with checking the device's dimensions and thickness, the equipment is also examined for precision and precession. Inspectors examine the labelling and calibration as well.

These devices are produced under the careful supervision of the Food and Drug Administrations (FDA) because they may have a number of safety concerns. At regular periods, FDA inspects the production facilities. [11]

MECHANISM OF NEEDLE FREE INJECTION TECHNOLOGY

The principle behind needle-free injection technology is to push the medicine quickly through a small aperture that is pressed up against the skin.

Needle-free injection technique uses the force produced by a compressed gas, such as air, carbon dioxide (CO2), or nitrogen (N2), to drive the medicine at high velocity via a small orifice. This enables skin penetration without the use of a needle thanks to an ultra-fine jet of high-pressure fluid. The diameter of orifice is smaller than diameter of skin.

The medicine is delivered to the skin, subcutaneous tissue, and intramuscular tissue in a fraction of a second when it is injected through the skin by an ultra-fine stream of fluid that permeates the skin.[12 13]

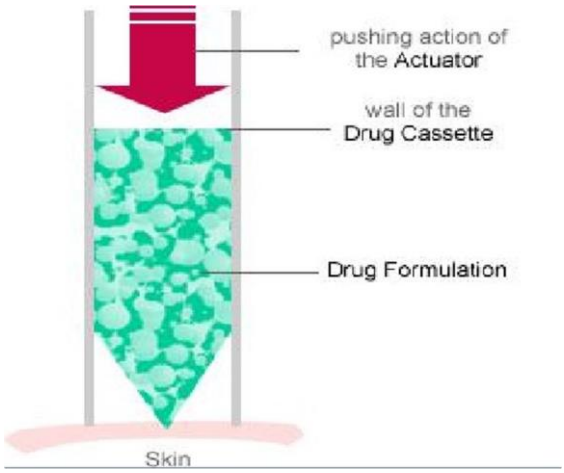

Figure 01: mechanism of working [14]

STAGES OF DELIEVERY:

There are three stages in the needle free drug delivery:

1. The peak pressure phase-optimal pressure used to penetrate the skin (<0.025 sec)
2. Delivery or dispersion phase (up to 0.2 sec)
3. Drop off phase (<0.05 sec)

The total amount of time required to deliver the vaccine is up to 0.5 seconds [15, 16]

MANUFACTURERS OF NEEDLE FREE INJECTION:

Mhi-500:

Mhi-500 is a novel needle-free insulin delivery system that benefits all those involved in diabetes care as well as those involved in clinical waste management. It is a viable substitute for needle-based delivery systems. This technology was approved by the Food and Drug Administration (FDA) in 1996 for subcutaneous insulin delivery and is CE marked for sale throughout Europe. This system has been used to successfully administer thousands of injections without the use of a needle. The mhi-500 injects insulin with a fine, high-pressure insulin jet.

Recojet:

Shreya Life Sciences recently launched Recosulin, a needle-free insulin delivery device, and recombinant human insulin under the brand name Recosulin. The new device is expected to improve the therapy because needle phobia was one of the factors preventing insulin use on a larger scale. In general, needle-free injection technology works by rapidly forcing liquid medication through a tiny orifice held against the skin. This produces an extremely fine stream of high-pressure fluid that penetrates the skin without the use of a needle.

Bioject's needle free injection technology:

Bioject's needle-free injection technology works by rapidly forcing liquid medication through a tiny orifice held against the skin. The orifice has a diameter smaller than that of a human hair. This produces a fine stream of high-pressure fluid that penetrates the skin without the use of a needle.

Bioject's technology is unique in that it can deliver injections to a variety of injection depths and accommodates a wide range of injection volumes. The Biojector 2000, for example, can deliver intramuscular or subcutaneous injections of up to one millilitre in volume. Furthermore, Bioject is working on a syringe for the Biojector 2000 that delivers intradermal injections and is currently in clinical trials.

Biojectorr 2000:

The system can also deliver subcutaneous injections and is being used in clinical trials for intradermal injections. The Biojector 2000 injects with sterile, single-use syringes, preventing cross-contamination that has been reported with fixed-nozzle jet injection systems. The Biojector 2000 has successfully administered over 10 million injections with no major complications reported. Because there is no needle, it offers healthcare workers unrivalled protection against accidental needle stick injuries. The Biojector injection system is ideal for high-risk situations, such as administering injections to HIV or hepatitis patients.

Vitajet 3:

The Vitajet 3 is a simple, low-cost needle-free injection system for delivering insulin. The system does not require any maintenance or re-assembly. The Vitajet 3 combines the quality of a reusable medical product with the convenience and safety of a sterile disposable, with disposable nozzles that are replaced once a week. The exclusive, easy-to-read Crystal Check disposable transparent nozzle allows to visually confirm loading and full discharge of insulin after each use and inspect the dosage prior to injection.

Cool click:

The cool click needle-free injection system was created by Bioject to deliver Saizen recombinant human growth hormone. Some children lack or produce insufficient amounts of naturally occurring growth hormone. To maintain normal growth, Saizen or growth hormone replacement must be injected. The system includes customised dosage features to accurately deliver variable doses of Saizen and was designed with bright colours to make the injector appealing to children while remaining nonthreatening.

SeroJet:

The SeroJet is a needle-free injection system that delivers Serostim recombinant human growth hormone for the treatment of HIV-associated wasting in adults. HIV-associated wasting is a metabolic condition in which HIV-infected people lose weight. This could lead to increased morbidity and mortality if not treated. Serono created Serostim to treat this condition by utilizing growth hormone's natural properties of increasing lean body mass. SeroJet is a customised version of Bioject's needle-free injection system Vitajet.

To accurately deliver variable doses of Serostim, the system includes customised dosage features.

Iject:

Bioject has developed the Iject, a second-generation gas-powered injector based on the design and performance of the B2000 and intended to be a single-use pre-filled device. In vitro testing has shown that the pressure profile of the Iject is nearly identical to that of the B2000, and injection performance of the two devices is thus predicted to be equivalent. The Iject is a single-use disposable injection device that comes pre-filled with 0.5 to 1.00 ml subcutaneous or intramuscular injections. The device is "ready to use" when it is delivered. [17, 18, 19, 20]

CLINICAL APPLICATION

A number of different drugs and vaccines have been delivered in humans using jet Injections. The first liquid jet injections for immunization were performed with multi-use nozzle jet injectors (MUNJIs), which permitted up to 1000 immunizations per hour of repeated injections of vaccine from the same nozzle and reservoir.They were successfully used to immunize people with vaccines against a variety of illnesses, such as polio, measles, smallpox, cholera, HBV, and a number of other diseases. The primary drawback of MUNJIs are subject to subject contamination which was discovered by spread of HBV. The World Health Organization suggests that due to the higher risk of contamination MUNJIs shouldn't be utilized for vaccination until all security concerns are taken care of. MUNJIs, on the other hand, should only be used for mass vaccination where the

benefits of rapid immunization outweigh the hazards of blood-borne infections, according to the Centres for Disease Control and Prevention. The World Health Organization advises against using MUNJIs for immunization until all safety concerns have been addressed due to the higher risk of contamination.

Jet injection has been used to deliver macro-molecules like hormones, monoclonal antibodies, and nucleic acids, but it has also been employed largely for the administration of vaccines. [21, 22]

THE FUTURE:

Many of these needle-free alternative technologies are still in the early stages of development. Companies are still working on making safer and easier-to-use devices. They are also developing alternatives that will allow them to deliver even more types of medicines. Inhalers, nasal sprays, forced air injectors, and patches are all being improved. Other foods may be genetically modified in the future to deliver vaccines and other drugs. Bananas and tomatoes are examples of such foods. In fact, bananas are being studied as potential carriers of a Norwalk virus vaccine. Tomatoes that are resistant to hepatitis B are also being researched Aside from new delivery systems, scientists are researching methods for producing longer-lasting drugs, which will reduce the number of needle injections.[23,24]

CONCLUSION:

Finally due to its painless nature needle-free technology is the best option for delivering medication into the skin without causing pain. Other advantages include much faster injection times when compared to conventional needles and no needle disposal issues. Not only can it help the pharmaceutical industry to increase product sales, but it also has the potential to improve compliance with dosage regimens and outcomes. Disease transmission through re-use of needles is a major issue in the developing world. There appears to be a major opportunity for needle-free technology to have a significant impact in the industry. Only when a large pharmaceutical or biotechnology company adopts needle-free technology and demonstrates its versatility, acceptance, and value in a major therapeutic area is it likely that dramatic change will occur.

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