International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

NEEDLE FREE INJECTION TECHNOLOGY

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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*

1. HISTORY

The first syringes were the first developed by a French surgeon, Charles Gabriel pravaz, in 1853, hypodermic there is a minor development in syringes is the technology has been remained unchanged for last 150 y.

Needle-free systems were the first described by marshalllockhart in 1936 in his patent jet injection.

Then in the early 1940's higson and others developed high pressure "guns"using a fine jet of liquid to pierce the skin and deposit the drug in underlying tissue.

2. INTRODUCTION

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

The future of this technology is promising ensuring virtually painless and highly efficient drug delivery. The major drawback associated with this technology is post administration "wetness" of the skin which may, if not taken care of, harbor dust and other untoward impurities. This technology is being backed by organizations as World Health Organization, Centers for Disease Control and Prevention and various groups including Bill and Melinda Gates Foundation.

This technology is not only touted to be beneficial for the pharma industry but developing world too find it highly useful in mass immunization programs, bypassing the chances of needle stick injuries and avoiding other complications including those arising due to multiple uses of single needle. Better patient compliance has been observed.

3. CLASSIFICATION OF NEEDLE FREE INJECTION TECHNOLOGY

1. On the basis of working.
   - Spring systems.
   - Laser powered.
   - Energy propelled system.
2. On the basis of type of load.

- Liquid.
- Powder.
- Projectile.

3. On the basis of mechanism of drug delivery.

- Nano-patches

4. On the basis of site of delivery.

- Intra dermal injectors.
- Intramuscular injectors.
- Subcutaneous injectors

4. DESIGN OF POWDER INJECTION SYSTEMS

These injections consist of a chamber filled with solid drug content and a nozzle for firing drug particles into the skin by utilizing the power source which typically is compressed gas. The injection has a diaphragm (a few microns thick) on either side of the chamber to cover the drug chamber.

Mechanism of powder injection:

- Particles exist from the nozzle along with a gas stream.
- Particles impinge the skin surface leading to the formation of a hole into the skin with the progression of the injection.
- Drug particles get deposited in a spherical pattern at the end of the hole and penetrate across the stratum corneum.
- After their penetration into the skin, drug particles get distributed completely into the stratum corneum and the viable epidermis.

Powder injection is accomplished by a light gas gun. It provides the required particle velocity by use of an accelerating piston which accelerates and carries particles with it. Particles leave piston surface by means of a deacceleration mechanism which slows down the piston. This leads to ejection of particles that act on the target tissue area.

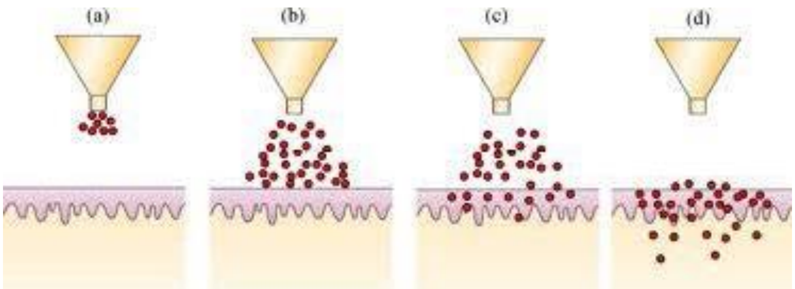

Fig. Mechanism of a powder injection

Ideal characteristics of powder particles:

- In case of powder, injections are the drug particle size distribution, quality, its physical and chemical stability are extremely important.
- Powder in an injection may be a whole drug or a formulation containing drug with excipients for dilution purposes or to stabilize the product. Therefore, drug and other excipients must be compatible with each other.
- Particle size are plays an important role in penetration into the stratum corneum; hence it should remain uniform throughout usage and storage.
- The particles must be robust enough to survive the highly energetic gas jet within the device as well as ballistic impact with the skin. As the particles strike the skin at a high velocity then they must be strong. The particles is clocked as fast as 900 meters per second, with 400 to 600 meters per second being the more typical range.
- In order to exert required effects in the body after being absorbed into systemic circulation, the drug particles should have proper diffusion within the skin.
- For skin penetration at a high velocity, the powders must have particle densities of about 1g/cc and mean diameter greater than 20 μm .

Powder needle free injection depends on being able to formulate the particles of sufficient density and accelerating them to sufficient velocity strong enough to penetrate the skin and in a quantity sufficient enough to reach the therapeutic dose levels . This was made successful by using helium as a power source assisted by modifications in the ways of the formulation of the drug.

Conversion of the drug either pure or along with excipients into hard particles of 10-50 nm in diameter, with a density approximately the same as a crystalline drug.

Coating the drug onto gold spheres which may act as a vector of few micrometres in diameter, this method is mostly applicable to DNA vaccines.

Design of liquid injection system:

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

Mechanism of liquid injections:

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

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

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

The accumulation of the liquid in the hole occurs because of a deeper hole in the skin which slows down the incoming jet. Then further development of a hole is stopped. The dimensions of the hole are established very early in the process from the time of impact. Stagnation of the jet at the end of the hole disperses the liquid into the skin in a near-spherical shape.

These systems are the designed for administration of a drug into muscles. They are creating a store of the drug into muscles that is released continuously over a desired time period [12].

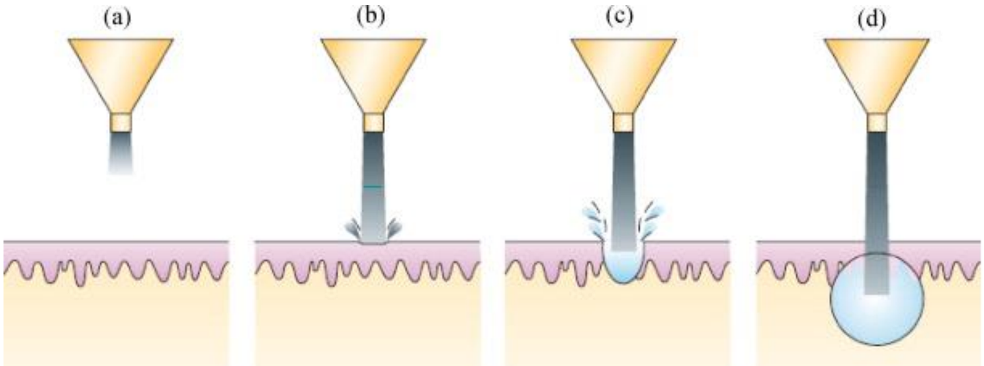

Fig. The mechanism of a liquid injection

Table: Market product of liquid-based needle free injection

Product name	Company	Types of system
Intraject	Weston medical	Liquid-based needle free injection
Medijector vision	Antares Pharma Inc.	Liquid-based needle free injection
Penjet	Penjet corporation	Liquid-based needle free injection
Med-E-Jet	Evans enterprise	Liquid-based needle free injection
Advantaget	Advantage health services	Liquid-based needle free injection
Gentlejet	Health for personal care	Liquid-based needle free injection
J-tip	National medical products, inc	Liquid-based needle free injection
Injex	Equidyne Systems, Inc	Liquid-based needle free injection
Powderject system	Powder ject pharmaceuticals	Powder-based needle free injection
DepixolDepo injection	Lundbeck Limited	Depot based needle free injection

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actual design and operation of the powder injection devices. These systems use gas or spring, pistons, drug-loaded compartments and nozzles. Typically, the nozzle has an orifice size of about 150 to 300 µm .

Mechanism of working of needle free injection system

Stages of delivery

There are three stages in the needle free drug delivery:

- The peak pressure phase-is optimal pressure used to penetrate the skin is<0.025 sec
- Delivery or dispersion phase is up to 0.2 sec
- Drop off phase is<0.05 sec

The total amount of time required to deliver the vaccine is upto 0.5 seconds.

5. COMPONENTS OF THE NEEDLE FREE INJECTION SYSTEMS

Nozzle:

The nozzle has the two significant functions it acts as the passage for the drug and as the surface which contacts the skin. The nozzle contains a flat surface and an orifice. The nozzle provides the surface which comes in contact in the skin and the orifice which has the drug passes through when injected. The orifice controls the drug stream diameter and speed. A stream diameter of approximately 100 µm and traveling at 100 m/s can achieve the desired injection depth of 2 mm

Drug reservoir:

The drug volume is holds the injection fluid inside the device.

Pressure source:

The energy source is provided to the essential driving energy to the drug for injection. Then many devices in the market use either mechanical or stored pressure as energy storage elements. The mechanical method stores energy in a spring which is released by pushing a plunger to provide to the necessary pressure. The pressure storage method is used to compressed gas in a vessel which is released at the time of injection .

Types of needle-free injection systems:

Needle-free injection systems are not a new development. The earliest systems were developed in the 1930s and used in a wide variety of medical areas over the years. 4 Through innovation and technology, there have been modifications and variations that allow for needle-free injection systems to be more widely available and effective to consumers.

- Spring load jet injector
- Battery powdered jet injector

- Gas powdered jet injector

Spring-load jet injector :

The spring-loaded jet injector uses is the spring mechanism that is drawn back. A trigger is then hit which release the spring creating a "jet stream" of vaccine or drug through the dermal layers of the skin. It is capable of subcutaneous, intramuscular or transdermal delivery. Each time the spring-load is activated the spring must then be manually redrawn to dose the next animal.

Battery-powered jet injector :

The battery-powered jet injector uses a small rechargeable battery pack to retract the dosing device. The dosing device has an electrical piston that is automatically redrawn after dosing. It is good for continuous use and minimizes worker fatigue. It is released by a small trigger. The injector resembles a battery powered hand drill. The battery-powered system administers subcutaneous, intramuscular or transdermal dosage depending on the recommended method.

Gas-powered jet injector:

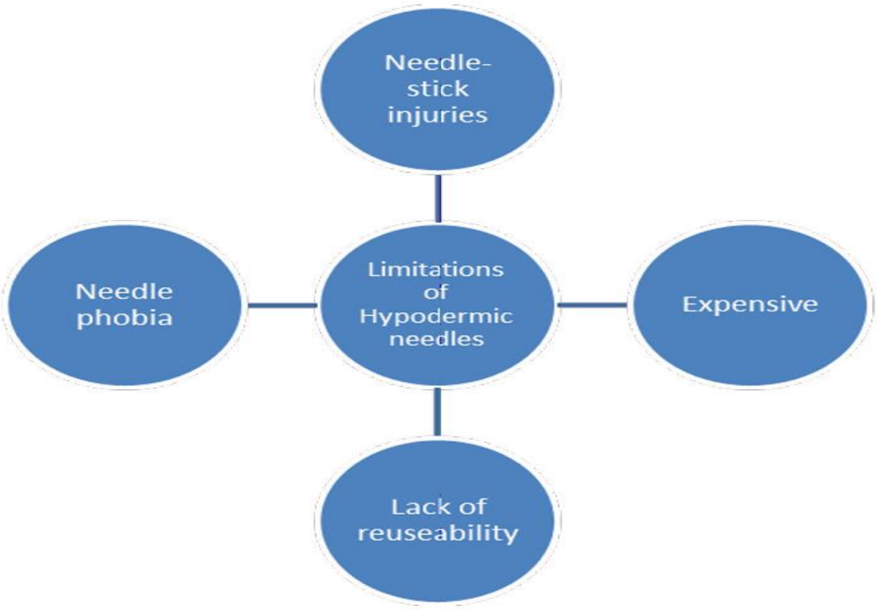
This type of injecting system was one of the first developed. It uses an gas or air cartridge attached to the gun either directly or indirectly through a tubing system to deliver power to the injector piston. When the trigger is activated it releases the piston and creates a jet stream of vaccine or drug subcutaneously, intramuscularly or Transdermally.

Advantageous of needle free injection:

- Prevent skin puncture hazards and its destruction; also does not cause the problem of bleeding or bruising and minimal skin response.
- Imparts fast drug delivery and better reproducibility as compared to invasive drug delivery systems and hence enhance bioavailability when compared with invasive drug delivery systems.
- Better drug stability during storage as it is delivered in dry powder form especially for water sensitive drugs.
- Avoids problems of reconstitution and any effect of shearing.
- Elimination of needle phobia.
- Self-administration is feasible with needle free injections.
- Improves immune response to vaccines. Immunization of influenza, tetanus, typhoid, diphtheria, pertussis, and hepatitis A vaccines can be delivered by needle free injections.
- Bio-equivalence has been demonstrated enabling the development of generic drug proteins

Disadvantages of needle free injection:

1. The method is complex and expensive.
2. All systems are not fitted into one size.
3. Need for personnel training and maintenance.
4. It is not applicable for the Intravenous route.



6. CONCLUSION

The evolution of drug delivery system aiming to penetrate the skin has been dependent on the simple engineering concepts. One of the major drawbacks of such devices includes the associated pain.

The use of the hypodermal needle in the traditional two-piece syringes has added to the woes.

Needle phobia and accidental needle-stick injuries have not only worsen patient compliance, but even unnecessary problems have surfaced.
Needle free technology are capable of delivering a wide spectrum of medicinal formulations into the body with the same bioequivalence as that which could have been achieved by drug administration by a two-piece syringe system, without inflating unnecessary pain to the patients.
These devices are very easy to be used, don't require any expert supervision or handling, easy to store, and dispose.
These devices are suitable for delivery of drugs to some of the most sensitive parts of the body like cornea. They are efficient to administer intra-muscular, subcutaneous and intra-dermal injections.

These systems require a power source which may be obtained either physically or by the application of some force.
The drug is forced and is ejected through a superfine nozzle at speeds near about to that of sound.
A great deal of investment has been made in developing this technology with several devices already being available in the market post FDA clearance.

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