# A Review On Needle Free Injection

**Savita Gavit,**
M Pharm Department Of Pharmacology,
Indira College Of Pharmacy Tathawade, Pune
**Sominath Thorave**
M Pharm Department Of Pharmaceutics,
Dattakala College Of Pharmacy Daund , Pune

## Abstract :

At present scenario many researches are working to develop technology that promises to develop technology that promises to deliver the drug in more efficient and less painful way in order to produce the therapeutic effect. Needle free injection technology was developed to reduces the number of needle sticks accident and associated problems.A comprehensive literature review was completed regarding needle free injection technology and it‟s application, advantages ,over needle injection and their componates and types such as powder injection , liquids injection , depot injection. Needle free injection system are novel ways to introduce various medicine into patients piercing the skin with a conventional needle.

Needle free injection gives very effective injection for a wide of drugs. Additional benefits includes very fast injection compared with conventional needle no needle disposal issue. This review intends to thought light on the basis mechanism by which this technology works, different types of technologies available at presents and its application. ( Chauhan, N.,et.al,2017.)

**Keywords:** Microjets, needle free devices, needleless injection, powder jets, pulsed microjets, shock waves.

## Introuction :

At present scenario, many researchers are working to develop technology that promises to make the administration of medicine more efficient and less painful. There are a variety of problems associated with the hypodermic needles used in injections. These include relatively high cost of the needles, lack of reusability i.e. needle syringe should be sterilized, additionally; many people have a fear of needles or needle-phobia, which causes them to avoid treatment.

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,They can take the form of power sprays, edible products, inhalers, and skin patches. While hypodermic needles were first introduced during the 1800s, needle-free systems are relatively recent inventions. Today, they are a steadily developing technology that promises to make the administration of medicine more efficient and less painful.

These technologies have been developed for injecting liquid formulations, as well as injecting drugs and vaccines in a solid dosage form. These devices were used extensively to inoculate against infectious diseases and were later applied more generally in large scale vaccination program.

The term „needle free" is used to describe an extensive range of drug delivery technologies, which consists of technologies that do not have a needle but make use of electrophoresis to drive drugs through the skin, technologies that use one or more very small needles, but needles nevertheless. Needle-free injection (NFI) systems are novel ways to introduce various medicines into patients without piercing the skin with a conventional needle. Injections are a popular mode for delivering drugs in order to prevent and treat various diseases. But it is an invasive method of drug administration as it causes tissue damage. Injections can be a source of disease transmission, particularly when needles are reused and used incorrectly. To overcome obstacles related to needle-based injections, needle- free injection technologies have gained popularity during the past few years and offer many benefits.

Many companies have developed alternatives to needle injections. Different designs which are included in this technology are nasal sprays, nose drops, flavored liquids, skin patches, air forced and edible vaccine-packed vegetables. In the near future, genetically enhanced foods may prove as an alternative for the delivery of vaccines.

Injections are a popular mode for delivering drugs in order to prevent and treat various diseases. But it is an invasive method of drug administration as it causes tissue damage. Injections can be a source of disease transmission, particularly when needles are re-used and used incorrectly.

The main goal for the delivery of any drug therapy is oral administration with once or twice daily dosing. However, there are large numbers of therapies, particularly protein-based, genebased, vaccine-based that cannot be delivered by this route for example insulin, growth hormones and other similar biologics. Therefore the needle free injection is becoming a very interesting subject of study.

Although the concept of needle free injection is not new, its previous application has been limited by device complexity and contamination risk. The latest injections developed are, however patient oriented, easy to use, disposable and their use is expected to increase considerably. The first hypodermic syringe was developed by Charles GabreilParvaz in 1853 but the free needle systems are relatively recent inventions. Needle free infection system is novel way to introduce various medicines into patient without piercing the skin with conventional needle. They can take the form of powder sprays, edible products, inhalers and skin patches. Today they are readily developing technology that promise to make the administration of medicine more efficient and less painful. The new injectors promise to potentially deliver macromolecules such as vaccines and protein painlessly without the use of a needle, thus increasing patient comfort and compliance as well as removing the risk of needle stick injuries to health care workers.

People are given injections to protect them from influenza, tetanus, cholera, typhoid, and other diseases. When a needle is inserted through the skin, the vaccine or drug it carries provides systemic immunity.

This is because the vaccine gets into the bloodstream and provokes the body to create antibodies that are carried throughout the entire body. Unfortunately, there are a variety of problems associated with the hypodermic needles used for these injections. One of the most significant drawbacks is the relatively high cost of the needles. The cost results in a lower vaccination rate, especially for children in developing countries. Another problem with traditional needles is the lack of reusability. If a needle syringe is not sterilized, reusing it can lead to the spread of disease. Additionally, many people have a fear of needles which causes them to avoid treatment. These drawbacks have led to the development of alternative delivery systems to needle injections.( Waghmare, P.V.,et.al,2014.)

## Literature Review:

1. **Dukare, M.V.,et.al,(2018):** Needle free injection system are to introduce the various medicines into patients without piercing the skin with a conventional needle. Needle-free technology offers the many benefit of reducing patient concern about the use of needle. Needle free injection is the very effective injections a wide range of drugs and bioequivalent to syringe and needle. It results in less pain, and is strongly preferred by patients. Additional benefits include very fast injection compared with conventional needles and no needle disposal issues.

2. **Kale,T.R.,et.al,(2014):** Needle free injection technology was developed to reduce the number of needle stick accidents and associated problems. A comprehensive literature review was completed regarding needle free injection technology and its applications, advantages over needle injections, their components and types such as powder injection, liquid injection, depot or projectile injection. This review describes needle free injection technology involving the generation of force by using compressed gas upon actuation in order to deliver a drug at very high speed through a nozzle.

3. **Waghmare P.V.,et.al,(2014):** A new generation of needle-free vaccine delivery devices (jet injectors) has been developed in an effort to decrease the risks of needle stick injuries to healthcare personnel and to prevent improper reuse of syringes and needles. Needle-free technology offers the very obvious benefit of reducing patient concern about the use of needle. Needle free injection gives very effective injections for a wide range of drugs and bioequivalent to syringe and needle, results in less pain, and is strongly preferred by patients. Additional benefits include very fast injection compared with conventional needles and no needle disposal issues.

## Histrory :

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.

Needles are painful due to their thickness, which is mostly required for structural reasons. The first air-powered needle-free injection systems were developed during the 1940s and 1950s for mass administration of vaccines to US soldiers.

These first injectors used compressed gas propel milliliters of liquid into the skin, even into muscle. These devices were gunshaped and used propellant gases to force fluid medicines through the skin. The obvious benefit of this research is to eliminate pain from injections. Today, there are commercially available jet injectors that derive from these military prototypes, like the Biojector from Bioject Inc. Needle injection of drugs is one of the most invasive methods of drug administering, it damages the tissue which may not heal in case of patients with diabetes, and in case of careless injection a patient can die from administering tiny bubble of air into a vein, infection or inflammation, it also is painful if performed improperly, also it is very hard to control the amount of drug administered by an injection and can cause an overdose and in some cases death.( Al-kaf, A.G.A.et.al,2014.)

## Objective:

1. To review needle vs. needle-free injection systems and describe the different types of needle-free injection systems.

2. Less Painful and Potentially Safer

3. The key benefits of avoiding a needle and ease of use of a liquid jet injector do not outweigh the overall cost of goods compared with other delivery technologies.

4. Major advantages of needle-free systems are the elimination of broken needles, a more constant delivery of vaccines and drugs, and decreased worker safety risk.

5. The aim of this review was to evaluate and summarize the evolution of jet injection intradermal drug delivery method including technological advancements and new indications for use.

## Structure of Skin:

The skin is one of the largest organs in the body in surface area and weight. The skin consists of two layers: the epidermis and the dermis. Beneath the dermis lies the hypodermis or subcutaneous fatty tissue.

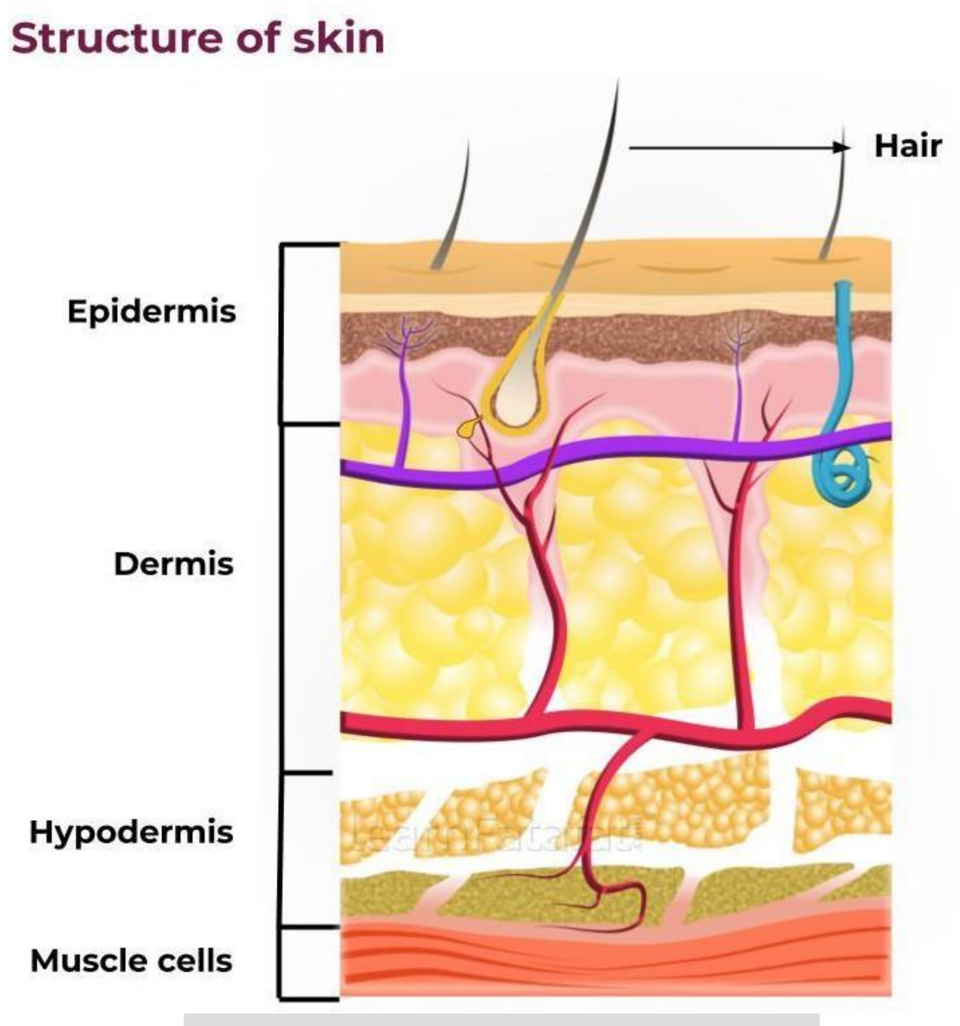


**Fig: 1: Structure of skin**

## Epidermis:

The epidermis, the outermost layer of skin, provides a waterproof barrier and creates our skin tone. It forms the waterproof, protective wrap over the body"s surface and is made up of stratified squamous epithelium with an underlying basal lamina. There are no blood vessels in epidermis, and cells in the deepest layers are nourished by diffusion from blood capillaries extending to the upper layers of the dermis.

## Dermis:

The dermis, beneath the epidermis, contains tough connective tissue, hair follicles, and sweat glands. The dermis is tightly connected to the epidermis by a basement membrane. The blood vessels in the dermis provide nourishment and waste removal from its own cells as well as from the stratum basale of the epidermis.

## Hypodermis:

The hypodermis is not part of the skin, the deeper subcutaneous tissue (hypodermis) is made of fat and connective tissue. Its purpose is to attach the skin to underlying bone and muscle as well as supplying it with blood vessels and nerves. It consists of loose connective tissue and elastin.( Dukare, M.V.,et.al,2018.)

## Components of needle free injection devices:

Devices may vary in design depending upon the drug for which they are used.

## 1. Injection device:

It consists of a drug chamber and made up of plastic. Sterility is maintained throughout the device.

## 2. Nozzle:

The nozzle serves as passage for the drug. It has an orifice through which the drug enters skin after injection. The diameter of orifice typically is 100 µm. The nozzle fires drug particles at a typical speed of 100 m/s with a depth of 2 mm. Thus this injection is painless; the patient feels tap of gas on the skin which is like flicking finger against the skin.

## 3. Pressure source:

The pressure source can be a mechanical method, stores energy in a spring and is released by pushing a plunger to provide the necessary pressure. It is important for delivering a drug forcefully into the systemic circulation via the skin. The most popular gases used in devices are carbon dioxide or nitrogen.

## Mechanism:

The mechanism generates force by using compressed gas (such as carbon dioxide or nitrogen)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 penetrates through the skin layers which deliver the drug very quickly into the systemic circulation. The total time required to deliver an injection is less than 1/3 of a second and occurs in three stages:

**Stage 1:** the peak pressure phase, optimal pressure used to penetrate the skin (< 0.025 sec).

**Stage 2**: the delivery or dispersion phase (~ 0.2 sec).

**Stage 3:** the drop-off phase (< 0.05 sec).

This pressure profile is consistent with each administration of vaccine ensuring each animal is vaccinated at the proper tissue depth. The needle-free injection technology improves the dispersion of medication throughout the tissue. As the fluid stream forces it‟s way through the tissue, it follows the path of least resistance, resulting in a widely dispersed, spider-web-like distribution of the medication.( Kumar, R.B.,et.al,2012.)

## Types Of Needdle Free Injection System:

1. **Powder injections**

These consist of a solid drug content filled in chamber and a nozzle for firing drug particles into the skin by utilizing compressed gas as the power source. A small volume of material, shot through the skin as drug, is in powder form instead of liquid form, hence injection is painless. The injection has a few microns thick diaphragm on either side of the chamber to cover the drug chamber.

The sustained release effect or drug performance can be achieved by using bio erodible carriers, slowly dissolving excipients specific, less soluble salts or dissolution aids. Protein drugs are very potent, and suitable for powder needle fee injection systems.

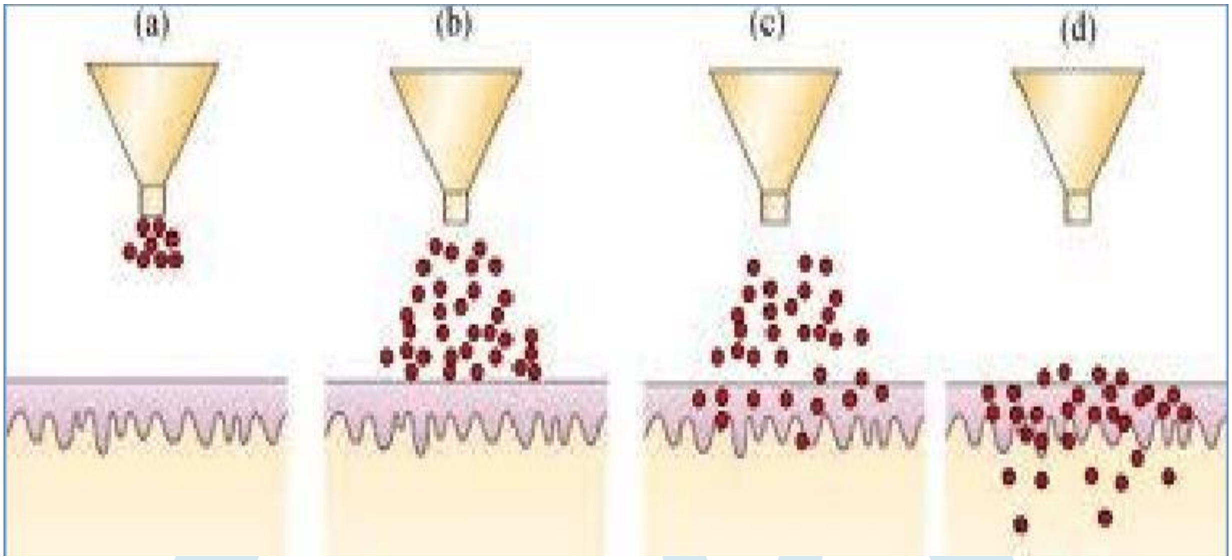


**Figure1: Mechanism of Action of powder injection.**

## 2. Liquid injections :

The basic principle of this injection is generation of high enough pressure by a fluid in intimate contact with the skin, to deliver liquid by punching a hole into the skin These systems use gas or spring, pistons, drug loaded compartments and nozzles having orifice size of about 150 to 300 μm.

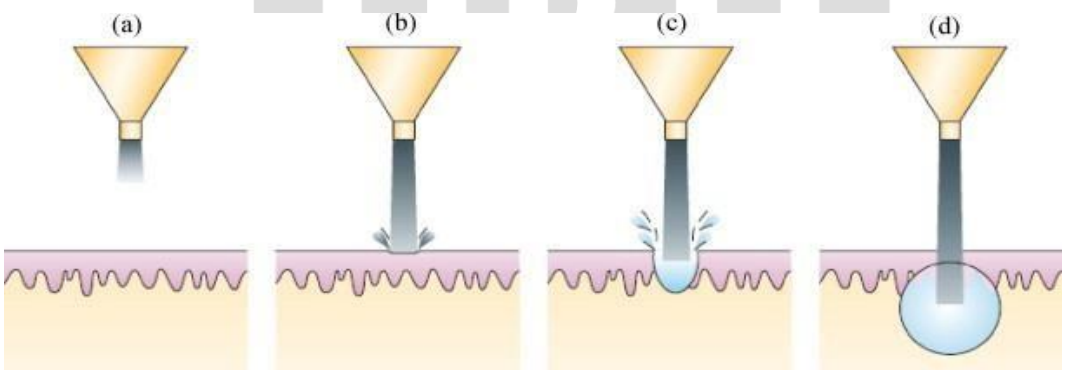


**Figure** :(2) **Mechanism of Action of Liquid injection**.

## 3. Depot or projectile injections:

These are designed for administration of a drug into muscles. They create a store drug into muscles that is released continuously over a desired time period.( Kale, T.R.,et.al,2014)

## Types of injections:

The needleless injections are mainly categorized into three types on the basis of the power source used in it.

### 1) Spring loaded injector:

The spring loaded injector uses a spring mechanism which is drawn back to push the drug into the underlying tissue where the drug dissolves and is released into the blood stream. The activated spring load must be redrawn manually for the next administration. Examples includes Dermojet ,Medi-jector.

### 2) Battery powered injector:

Use of electricity as source of energy. It consists of a small rechargeable battery pack to retract the dosing device. The dosing device has an electric piston which is automatically redrawn after dosing. It is used for subcutaneous, intramuscular or transdermal delivery of drug. Examples include intradermal application of liquids

### 3) Gas powered injector:

This type in injecting system was one of the first developed .it uses and gas or air cartridge attached to the gun either directly and indirectly through tubing system to deliver powder to the injector piston.

## ClasscificationOf Needle Free Injection Technology.

1. On the basis of working.

- Spring systems.
- Laser powered.
- Energy propelled systems.
- Lorentz force.
- Gas propelled/air forced.
- Shock waves.

2. On the basis of type of load.

- Liquid.
- Powder.
- Projectile.

3. On the basis of mechanism of drug delivery.

- Nano-patches.
- Sandpaper assisted delivery.
- Iontophoresis enabled.
- Micro-needles.

4. On the basis of site of delivery.

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

## Recent Needle-Free Injection Technologies

### 1. Serojet.

The device is designed for delivering Serostim recombinant human growth hormone administered subcutaneously. The Serojet device is tailored from Vitajet technology. This is used for treatment of HIV associated wasting in adults and was approved by FDA in March 2001 for marketing


**Fig: Serojet**

## 2. Iject

It is a product of the Bioject Company as a second generation gas powdered injection system. The Iject is a pre-filled single-use disposable injection device configured to administer 0.5 to 1.00 ml subcutaneous or intramuscular injections. The device is initiated by rotating the trigger sleeve 180 degrees. By advancing the trigger sleeve, the injection is administered, where the nozzle is placed injection site.

**Fig :Iject**

## 3. Injex

Injex system offers administration of local anesthesia. It consists of an injection ampoule having orifice of 0.18 mm. From this orifice, the drug is fired under dosed pressure into the submucosa. The ampoule must be placed on the attached gingiva at an angle of 90° directly above the tooth to be anaesthetized. The local anesthetic volume that can be administered is about 0.3 mL


**Fig :Injex**

## 4. Bioject®Zetajet:

It consists of two components, the portable injector and an auto disabling disposable syringe. It is intended to deliver vaccines and injectable medications either subcutaneously or intramuscularly and is indicated for both professional use and home use for patients who self-inject. The syringe assembly has a unique "auto-disable" feature that prevents re-use of the syringe.

disable" feature that prevents re-use of the syringe


**Fig:Bioject.**

## 5. Cool click:

Bioject developed it for delivering Saizen recombinant human growth hormone. In some children, naturally occurring growth hormone is absent or is produced in inadequate amounts. In these cases, Saizen or growth hormone replacement must be injected to maintain normal growth.


**Fig : Cool Click**

## 6. Vitajet

It received FDA approval for marketing in 1996. It consists of disposable nozzles which are replaceable once in week and used for delivery of insulin subcutaneously

**Fig :Vitajet**

## 7.Mhi-500:

This device is used for subcutaneous administration of insulin. The system was approved by FDA in 1996 and for sale throughout Europe. The device creates a fine jet of insulin through the nozzle penetrating skin tissues of the subcutaneous layer.

## 8.Madajet:

It is commonly used in dentistry. It works by using pneumatic pressure to discharge local anesthetic. This stream makes a wheel of about 5 to 6 mm in diameter at the base of injection. The device injects a volume of 0.1 cc per injection intradermally.( Mohizin, A.,et.al,2018.)

## Problems it solves:

1. Avoids needle stick hazard.
2. No sharps disposal problems.
3. Eliminates the concern for the re-use of needles.
4. Injection pain is reduced in most cases.
5. Speeds the injection cycle.

6. Improved bio-availability of vaccines.
7. Reduces the system cost of injection.
8. Key Needle Free Manufacturers of the World.

## Advantages :

1. No under- or overdosing condition of the drugs
2. Useful in case of patients with needle phobia.
3. It delivers pain-free injection. Prevents skin puncture hazards and its destruction; also does not cause problem of bleeding or bruising and minimal skin response.
4. Improved patient compliance especially in chronic administration of drugs.
5. No need to visit hospitals / experts for injections, i,e., self-administration is feasible.
6. No specific disposal requirements.
7. No risk of cross contamination from needle-stick injury.
8. Amount of medicine delivered and the depth can be adjusted.
9. Vaccines can be delivered in powdered form as well as viscous liquids.
10. Better drug stability during storage as it is delivered in dry powder form.

## Disadvantages :

1. Method is complex and expensive.
2. All systems are not fitted into one size.
3. Need for personnel training and maintenance.

## Applications :

The following are the drugs which are widely used with this technology.

1. Insulin, which is to be administered several times during the day is considered to be the best candidate for needleless delivery.
2. Lidocaine hydrochloride, a local anesthetic is suitable to be delivered needle free.
3. Heparin (an anticoagulant), erythropoietin, lidocaine hydrochloride (a local anesthetic)

and various vaccines can be administered through needleless injection. This technology has been tried with several newer drugs to delivery them in a patient compliant way and has been successful in most cases.( Ravi, A.D.,et.al,2015.)

## Disscusion:

Needle-free injection is a medical technology that delivers medication into the body without the use of needles. It has gained popularity in recent years due to its advantages over traditional needle-based injections, such as reduced pain, decreased risk of infection, and easier administration.

One of the most commonly used needle-free injection technologies is the jet injector. This device uses high-pressure air or gas to create a fine stream of medication that penetrates the skin. However, jet injectors can cause discomfort due to the force of the injection, and they can also lead to bruising or bleeding in some cases.

Another type of needle-free injection is the micro-needle patch. This technology uses a patch containing microscopic needles that penetrate the skin and dissolve, delivering the medication directly into the bloodstream. Micro-needle patches are painless and have a lower risk of infection, but they can be more expensive than other injection methods.

A third type of needle-free injection is the ballistics method, which uses a high- velocity spray of medication to penetrate the skin. This method is relatively painless and has a low risk of infection, but it can be messy and less precise than other injection methods.

Overall, needle-free injection has several advantages over traditional needle-based injections. It can reduce pain and anxiety, improve patient compliance, and decrease the risk of infection.

# Conclusion:

Needle-free injection systems have potential to improve efficiencies. Major advantages of needle-free systems are the elimination of broken needles, a more constant delivery of vaccines and drugs, and decreased worker safety risk. Needle free injection technology offers effective injectors for a wide range of drugs & bioequivalent to needles and syringes.

There appears to be tremendous opportunity for needle-free technology in pharmaceutical industry. Needle Free Injectors are easier to use, more efficient, more reliable, much safer and have no disposal problems. Additional benefits include very fast injection as compared with conventional needles.

The biotech revolution is bringing in a range of protein-based therapeutics into the marketplace at rapid pace-more than 300 products in active development. These protein-based therapeutics especially monoclonal antibodies (MAbs), which are anticipated to represent 30 per cent of pharmaceutical sales by 2007 and which are otherwise challenging to deliver non-invasively, will continue to be formulated as injectables.

It is likely that dramatic change may occur only when a large pharmaceutical or biotechnology company adopts needle-free technology and demonstrates its versatility, acceptance and value in major therapeutic area.

## Reference:

**1.** Chauhan, N., Kumar, K. and Pant, N.C., 2017. An updated review on transfersomes: a novel vesicular system for transdermal drug delivery. *Uni J Pharm Res*, *2*(4), pp.42-45.

**2.** Waghmare, P.V., Chinchole, A.S., Chavan, D.V. and Bhusnure, O.G., 2014. A Review on Needle-Free Inj. Systems: Novel Approach to Drug Delivery, 4(2), pp. 38 – 40.

**3.** Al-kaf, A.G.A. and Othman, A.M., 2017. A review on needle free injections. *Uni J Pharm Res*, *2*(2), pp.5-7

**4.** Dukare, M.V. and Saudagar, R.B., 2018. Needle free injection system. *Int J Curr Pharm Res*, *10*(2), pp.17-24.

**5.** Kumar, R.B., 2012. Needle free injection systems. *Pharm. Inno*, *1*(9), pp.30-35.

**7.** Kale, T.R. and Momin, M., 2014. Needle free injection technology-An overview. *Inno Pharm*, *5*(1),pp.56-60.

**8.** Mohizin, A. and Kim, J.K., 2018. Current engineering and clinical aspects of needle-free injectors: A review. *J Mech Sci Tech*, *32(3)*, pp.37-47.

**9.** Ravi, A.D., Sadhna, D., Nagpaal, D. and Chawla, L., 2015. Needle free injection technology: A complete insight. *Int J Pharm Inve*, *5*(4), p.192.

**10.** Trimzi, M.A. and Ham, Y.B., 2021. A needle-free jet injection system for controlled release repeated biopharm. Deliv *Pharm,13*(11), pp.17-30.

**11.** Kumar, R.B., 2012. Needle free injection systems. *The Pharma Inno.1*(9), pp.25-30.

**12.** Houser, T.A., Sebranek, J.G., Baas, T.J., Thacker, B.J., Nilubol, D. and Thacker, E.L., 2003. Feasibility of transdermal, needleless injections for prevention of pork carcass defects. *Iowa Sta Uni Animal Ind Report*, *1*(1), pp.30 – 45.

**13.** Kaur, J., Srivastava, R. and Borse, V., 2021. Recent advances in point-of-care diagnostics for oral cancer. *Biosen Bioele 178(4)*, pp.11-29.