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Review Article

# Needle free injection device: The painless technology

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**ABSTRACT**

Today there are readily developing technologies that promise to make the administration of medicine more efficient and less painful. Needle free- injection device are injections developed to be patient oriented, easy to use, disposable and their use is expected to increase considerably. It solves the problems created due to conventional needles making them safer, less expensive, and much more convenient for medication purpose. Needle free injection gives very effective injections for wide range of drugs and is bioequivalent to syringe and needle, results in less pain, and is strongly preferred by patients. Basically the aim of modern needle-free drug delivery system is to enhance the prescribing and adoption of important drugs that require self-injection.

## 1. INTRODUCTION

Needle-free injection systems are novel ways to introduce various medicines into patients without piercing the skin with a conventional needle [1]. Needle free injection device (NFID) gained popularity during the past few years as a beneficial technology that has been meant for injecting liquid formulations, as well as injecting drugs and vaccines in a solid particle dosage form. Devices are available in reusable and disposable forms, for home or physician's office use, and also in versions for multiple patients and institutional uses [2].

Drug delivery plays a pivotal role in the field of human health care where nearly 12 billion injections are administered annually for medical purposes 3% of which are used for immunization. Throughout the world, 0.7% of deaths and 0.6% of disability-adjusted life years (DALYs) are caused by contaminated injections in health care settings [3]. According to Food and drug administration [FDA] a needle-less or needle free injection is a device used for the parenteral administration of a medicament. Needle-free injection offers a fast, effective route of administration. Additional benefits include very fast injection compared with conventional needles and no needle disposal issues. Not only it can benefit the pharmaceutical industry in increasing product sales, it has the added potential to increase compliance with dosage regimens and improved outcomes. However, there appears to be tremendous opportunity for needle-free technology to have major impact in the industry. It might take a dramatic change that may occur only when a large pharmaceutical company adopts needle-free technology and demonstrates its versatility, acceptance and value in major therapeutic area. 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.

The main objective of needleless injection is to avoid the risks and complications involved in conventional needles and to be used in diseases like diabetes, skin disease, allergy, asthma,etc. as a drug delivery system. The key benefits are avoiding a needle and ease of use of a liquid jet injector. The main advantage of this system is the elimination of broken needles, a more constant delivery of vaccines and drugs, and decrease worker safety risk. Sterility is a key factor to proper vaccination and drug delivery. Sterility can be affected by human error. Needle-free injection takes the needle out of the equation, and due to the high powered dosing mechanism, there is a little to no chance of cross contamination [4].

Needle free drug delivery was first projected in the early 19th century with one of the key patents filed by Lockhart in 1930 [5]. The first needle free injection systems which were present in the form of air powered devices were developed during the 1940s and 1950. 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. These devices were used extensively to inoculate against infectious diseases and were later applied more generally in large scale vaccination program.

### 1.1 Advantages of needle-free injection over current needle injection

- Prevent skin puncture hazards and its destruction
- Does not cause problem of bleeding when skin get injures or ruptured.
- Imparts fast drug delivery and better reproducibility hence enhance bioavailability when compared with needle injection
- Excellent dose response is observed with increased drug doses
- Better drug stability during storage especially for water sensitive drugs.
- Elimination of needle phobia.
- Self-administration with needle free injections.
- Improves immune response to vaccines.
- Significantly decrease the spread of diseases and cross contamination i.e. sterility can be maintained
- Improved safety for workers by eliminating accidental needle sticks when using traditional needle-and-syringe administration.
- Rapid delivery of the drug to the systematic circulation
- Lower pain and stress

### 1.2 Disadvantages of needle-free injection [6]

- Method is complex and expensive.
- All systems are not fitted into one size.
- Need for personnel training and maintenance.
- It is not applicable for Intravenous route.

**Table 1.** Comparison between a Needle Free Device v/s Needle-Based Syringe Delivery

| S. No | Parameters compared | NFD Pharma-Jet | Needle/Syringe |
|---|---|---|---|
| 1. | Route of Administration | Intramuscular/ Subcutaneous | Intramuscular/ Subcutaneous |
| 2. | Volume | 0.5ml | 0.5ml |
| 3. | Orifice Inner Diameter | 0.010" | 0.0095" for 25 gauge (0.0035" for 33 gauge) |
| 4. | Barrel Inner Diameter | ~.25" | ~.25" – .5" |
| 5. | Stroke | ~1" | ~ 0.5" – 1" |
| 6. | Speed of Injection | ~.3–.5 sec | ~.3 – 1 sec |

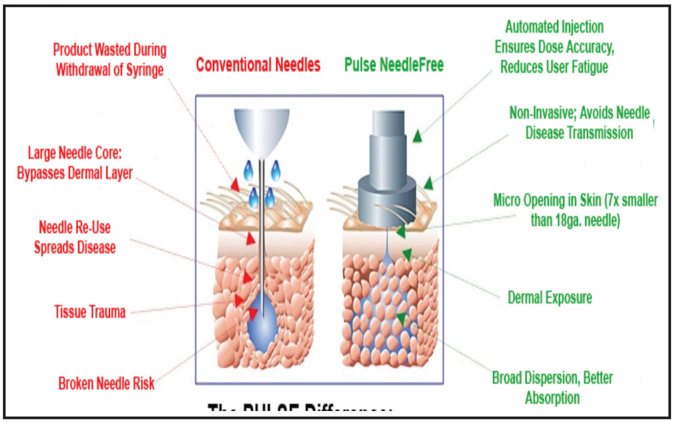


**Fig 2.** A comparison of conventional needle and needle free injection

## 2. COMPONENTS OF A NEEDLE FREE INJECTION DEVICE

It consists of injection device, drug reservoir, nozzle and pressure source.

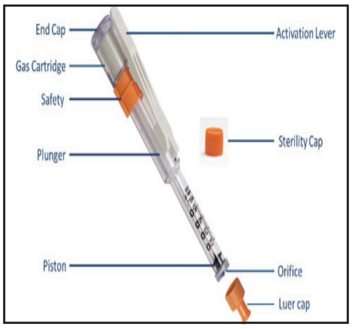


**Fig. 3.** Component of needle free device

### 2.1 Injection device

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

### 2.2 Drug reservoir

The drug volume holds the injection fluid inside the device

### 2.3 Nozzle

The nozzle serves as passage for the drug and serves as the skin contacting surface. The nozzle has an orifice through which the drug enters skin when injected. 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. The most common orifice size is 0.127mm, comparable to a 25-guage needle. Therefore this injection is painless; the patient feels tap of gas on the skin which is like flicking your finger against your skin.

### 2.4 Pressure source

It is important for delivering a drug forcefully into the systemic circulation via the skin. The pressure source can be a mechanical method which stores energy in a spring and is released by pushing a plunger to provide the necessary pressure. It can also be a pressure storage method that utilizes compressed gas in gas cartridge as shown in Figure. 3 the most popular gases used in devices are carbon dioxide or nitrogen. Pressurized metal air cartridges are often provided for access in portable units.

**Air-forced needle-free injection systems:** The air-forced needle-free injection systems are typically made up of three components including an injection device, a disposable needle free syringe and an air cartridge. The injection device is made of a durable plastic. It is designed to be easy to hold for self-administration of medicine. The needle-free syringe is also plastic. It is sterilized and is the only piece of the device that must touch the skin. The syringe is made to be disposed after every use. For portable units, pressurized metal air cartridges are included.

## 3. MANUFACTURING OF NEEDLE FREE INJECTION SYSTEM [7]

There are various methods of producing needle free injection system. The manufacturing process involves steps such as molding the pieces, assembling them, decorating and labeling the final product. All of the manufacturing process is done under sterile conditions to avoid the spread of disease.

a. Molding the pieces: It involves production of the component plastic pieces from plastic pellets. This is done by a process called injection molding.

b. Assembling and labeling the pieces: Pieces are inserted into the main housing and buttons are attached. Machines apply markings that show dose levels and force measurements.

c. Packaging: Injection devices are first wrapped in sterile films and then put into cardboard or plastic boxes. These boxes are then stacked on pallets

## 4. MECHANISMS OF WORKING OF NEEDLE FREE INJECTION SYSTEM

Needle-free injection technology works by forcing liquid medication at high speed through a tiny orifice that is held against the skin. The diameter of the orifice is smaller than the diameter of a human hair. This creates an ultrafine stream of high-pressure fluid that penetrates the skin without using a needle. The design of the device has a major influence on the accuracy of subcutaneous delivery and the stresses imposed on the product to be delivered. The design must ensure that a sufficiently high pressure is generated to puncture the skin, while the subsequent pressure is reduced to ensure that the molecule is deposited comfortably at a level that does not reach the muscle tissue. High-pressure delivery could potentially damage fragile molecules, such as monoclonal antibodies. Successful delivery of such molecules, therefore, requires a device with carefully controlled power nuance. Injection event requires less than 0.5 seconds and injections can be IM, SC or ID.

The needles free injection system can control all the parameters concerning drug delivery like reproducibility on any skin condition, optimizing absorption characteristics, amount of drug to be delivered, time of delivery and digitally controlled exfoliation accuracy.

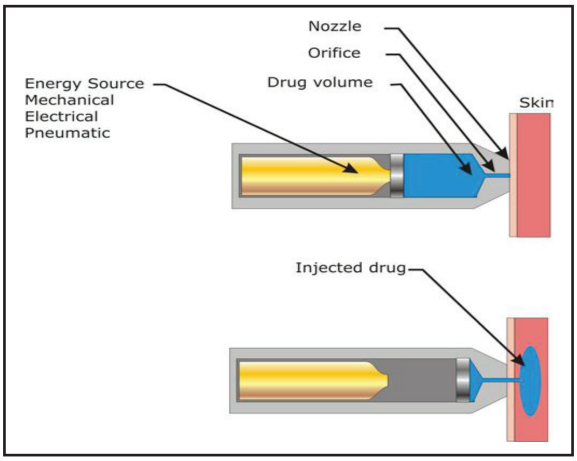


**Fig. 4.** Mechanism of working

There are three stages in the needle free drug delivery:

(*i*) The peak pressure phase-optimal pressure used to penetrate the skin (<0.025sec)

(*ii*) Delivery or dispersion phase- (up to 0.2 sec)

(*iii*) Drop off phase- (<0.05 sec)

The total amount of time required to deliver the vaccine is up to 0.5 seconds [9].

Medicaments can be injected by intra-muscular, subcutaneous and intra-dermal routes using needle free injections. Intramuscular injections are the deepest injection type, the medication is delivering into the muscle tissue. Most vaccines are currently delivered to the intramuscular depth. Subcutaneous injections are delivered to the adipose (fat) layer just below the skin. Many therapeutic proteins are delivered to the subcutaneous depth, such as human growth hormone. Intradermal injections are very shallow injections that deposit the medication between the layers of the skin. Many new DNA-based vaccines are delivered to the intra-dermal layer. Bioject's needle-free injection technology improves the dispersion of medication throughout the tissue; it follows the path of least resistance, resulting in a widely dispersed, and spider-web like distribution of the medication [11].

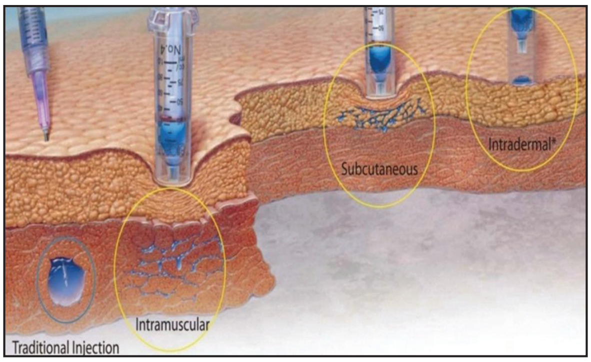


**Fig. 5.** Injecting medicament through skin by needle free injection

## 5. TYPES OF NEEDLE FREE INJECTION SYSTEMS

All these technologies have the same basic principle of delivering medication by pressurized contact of fluids with the skin. Needle-free injection drug delivery systems are classified as follows [12]

- Powder injections
- Liquid injections
- Depot or Projectile Injection

### 5.1. Powder injections

In powder injection systems, a pre measured powdered medication is put in a drug cassette which is opened by the compressed gas and thus the medication is delivered to tissue. The powders used in these systems require specific properties and specific size to ensure their stability and proper dispersion into the tissue. Two different methods are used for the drug formulation, the drug either alone or in combination with excipients is formulated as hard particles of 10-50μm in diameter having density equivalent to the crystalline drug [13]the latter, technique is used generally for DNA vaccines. Because the drug is administered in a solid dosage form, enhanced stability and potentially avoids the need for refrigeration or may not require cold chain storage, as well as providing the opportunity for controlled release formulations by using slower dissolving excipients. In these injection systems, the powders are processed by compression, milling, sieving, and more scalable methods like spray drying, freeze drying, fluid bed drying, spray coating of seed particles, solution filling and drying pre formed hydrogel beads and emulsion techniques to form erodible micro particles [14]. A wide range of proteins, peptides and small molecules can be delivered using the technology. Preclinical studies with a range of antigens have also shown improved efficacy for vaccines when compared to a standard needle and syringe injection.

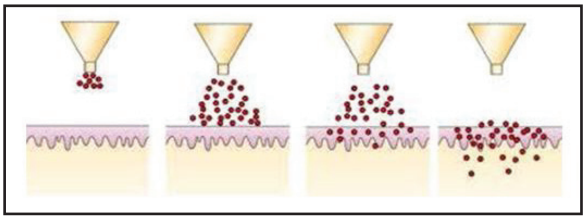

**Fig. 6.** Mechanism of a powder injection

### 5.2. Liquid injections

The basic principle of this injection is, if a high enough pressure is generated by a fluid, then the liquid will punch a hole into the skin and will be delivered into the tissues in and under the skin. As same principle is applied as in powder, there is a difference in the 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 [15].

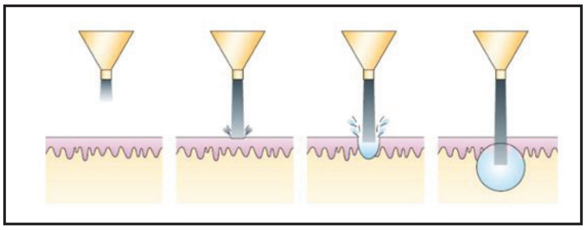

**Fig. 7.** Mechanism of a liquid injection

### 5.3. Depot injections

Depot injections are given in the muscle, where they create a depot of a drug that is released continuously over a specified period of time. It is a very recent advancement of the technology. The depot is driven into the skin with a sufficient force to penetrate the skin and fatty tissue. A typical depot is about 1mm in diameter [16] which is adequate for most proteins and antibodies. The pressure of 3-8 mega Pascal's (MPa) is enough to puncture the skin with a sharp tipped punch. This is particularly useful and advantageous for drugs that are affective in the milligram dose range, and if, liquid forms of the drugs are unstable.

## 6. APPLICATIONS OF NEDDLE FREE INJECTION DEVICE

(*i*) Intramuscular, subcutaneous and Intradermal administration of Vaccines e.g.., smallpox, polio, measles

(*ii*) Intradermal administration of hormones e.g..; growth hormone

(*iii*) Intradermal administration of anaesthetics e.g.., lidocaine

(*iv*) Subcutaneous administration of insulin

(*v*) Used in the treatment of migraine e.g.., sumatriptan

(*vi*) Animal Pharmaceuticals: e.g.., MS Pulse250 system is used

(*vii*) Used to deliver drugs (Weston medical) which consist of proteins, peptides, monoclonal antibodies, small molecules and vaccines.

## 7. RECENT TRENDS

### 7.1 Pulsed micro jets

Having a long history, needle-free liquid jet injectors are not commonly used as a result of frequent pain and bruising. It was hypothesized that pain and bruising originate from deep penetration of jets into skin leading to their interactions with nerves and blood capillaries. This issue could potentially be addressed by minimizing the penetration depth of jets into the skin; this issue was solved when a new strategy came into existences that are pulsed micro jets [17].

### 7.2 Micro jets

They were produced by displacing the drug solution through a micro nozzle (50–100 m in final diameter) by using a piezoelectric transducer. Other modes of fluid displacement, including dielectric breakdown and electromagnetic displacement, can also be potentially used however; the piezoelectric-based mechanism was preferred as a result of its robustness and energy efficiency.

### 7.3. Shock waves

The most efficient mechanisms of energy dissipation observed in nature. In this study, the instantaneous mechanical impulse generated behind a micro-shock wave during a controlled explosion are utilized for drug delivery. It is well-known that antigens in the epidermis are efficiently presented by resident Langerhans cells, eliciting the requisite immune response, making them a goodet for vaccine delivery. Unfortunately, needle-free devices for epidermal delivery have inherent problems from the perspective of the safety and comfort of the patient [18].

**Table 2.** Marketed needle free injection devices (NFID)

| S. No. | Product Name | Company | Type of systems |
|---|---|---|---|
| 1. | Intraject | Weston medical | Liquid based needle free injection |
| 2. | Medi jector vision | Antares Pharma Inc. | Liquid based needle free injection |
| 3. | Penjet | Penjet corporation | Liquid based needle free injection |
| 4. | Med-E-Jet | Evans enterprise | Liquid based needle free injection |
| 5. | Advantaget | Advantaget health services | Liquid based needle free injection |
| 6. | Gentlejet | Health for personal care | Liquid based needle free injection |
| 7. | J-tip | National medical products, inc | Liquid based needle free injection |
| 8. | Injex | Equidyne Systems, Inc | Liquid based needle free injection |
| 9. | Powderject system | Powderject pharmacueticals | Powder based needle free injection |
| 10. | Depixol Depo injection | Lundbeck Limited | Depot based needle free injection |

### 7.4 Biojector 2000

The Biojector 2000 is a durable, professional-grade injection system designed for healthcare providers. The Biojector 2000 uses sterile, single-use syringes for individual, which prevent the cross-contamination that has been reported with fixed-nozzle jet injection systems. Because there is no needle, the Biojector provides healthcare workers with an unparalleled level of protection against accidental needle stick injuries. In high-risk situations, such as delivering injections to patients known to be infected with HIV or hepatitis, the Biojector is an ideal injection system.

**Fig. 8.** Biojector 2000

### 7.5 Iject

Bioject has developed a second-generation gas-powered injector known as the Iject, which is based on the design and performance of the B2000 and is intended to serve as a single-use pre-filled device. The pressure profile of the Iject has been documented by *in-vitro* testing to be virtually the same as that of the B2000, and injection performance of the two devices is therefore predicted to be equivalent. 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 distributed “ready to use.” Thus, it requires no additional parts or modifications for function. The device is primed by rotating the trigger sleeve 180 degrees, and an injection is administered by advancing the trigger sleeve while the nozzle is held against the injection site. The Iject needle-freeinjection system is an investigational device, subject to the US Food and Drug Administration clearance for commercial distribution.

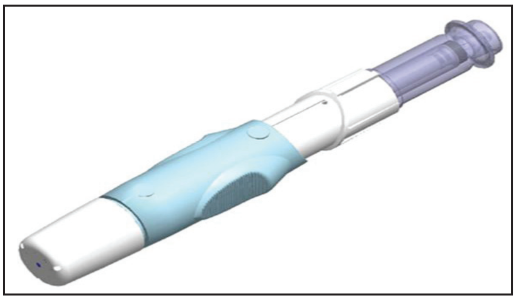

**Fig. 9.** Inject

### 7.6. Intraject technology

The device looks like fountain pen which is pre-filled and disposable. The device is suitable for liquid protein formulation. The drug delivery occurs by pushing actuator by using compressed nitrogen in less than 60 milliseconds [19].

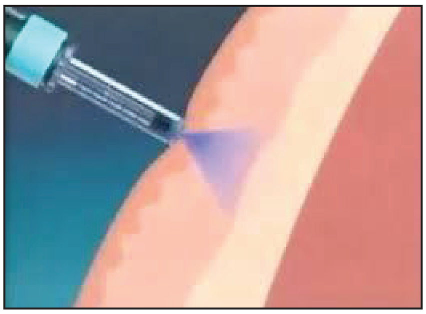

**Fig. 10.** Intraject

### 7.7 Biovalve's Mini-Ject technology

The device is simple to use, pre-filled, disposable. Device is suitable for delivering largeproteins, fragile antibodies and vaccines. Used for intradermal, subcutaneous and intra-muscular administration

**Fig. 11.** Biovalve's Mini-Ject

## 8. THE FUTURE PROSPECTIVE OF NFID

Many of the needle free technologies are in the growth stage. Companies are working on producing devices that are harmless, easier to use & can deliver more types of medicines. Inhalers, nasal sprays, forced air injectors and patches are being developed. In the near future, genetically enhanced foods may prove as an alternative for the delivery of vaccines and other drugs. These include foods like bananas and tomatoes. Actually, bananas are looked as carriers for vaccines to defend against the virus and for protection against hepatitis B. Besides these novel delivery systems, scientists are also investigating methods for producing long lasting drugs that will minimize the number of needle injections [20].

## 9. CONCLUSION

The needle free technology gives the very benefit of minimizing patients fear regarding the use of needle. Many of other benefits comprise very fast injection as compared to traditional needles and needle disposal issues are rarely seen. It can assist the pharmaceutical industry in rising product sales. It also has the extra potential to increase conformity with dosage regimens and enhanced outcomes. Needle free injection systems are customizable to each operation and can be modified to optimize productivity. Various supporting organizations and groups are involved in the advancement of needle free alternatives for drug delivery. The biotech revolution is bringing a series of protein based therapeutics into the market place at rapid speed. The use of needle free system can be challenging. Workers require training and education regarding any new technique. Start-up and training costs may also affect the interest in this technology.

## REFERENCES

[1] Houser TA, Sebranek JG, Bass TJ, Thacker BJ, Nilubol D, Thacker EL. Feasibility of transdermal, needleless injections for prevention of pork carcass defects. Meat Science. 2004: 68(2); 329-332.

[2] Gupta MM, Kumar V, Basniwal PK. Needle Free Injection: An Alternate Approach of Injection. The Pharma Review 2008: 37-41.

[3] Kadam V, Mundhe B, Shahane A, Ingole B. A Review on Needle-Free Injection System. WJPPS 2014; 3(3): 763-780.

[4] PQA Plus. Available at http://www.pork.org/filelibrary/PQAPlus/PQAPlusEdBook.pdf.Accessed September 21, 2011.

[5] Lockhart M. U.S.Patent No. 69,199, March 16, 1936..

[6] Daniels CS. Needle-Free Injection: Pros and Cons. Available from: URL: http://www.highplainsdairy.org/2010/9_Daniels_Needle%20Free%20Injection_FINAL.pdf,accessed on 15th January 2014

[7] Hirlekar R, Jose P. Needleless Injection System. IJPCS 2013; 2 (4):1857-1863.

[8] Tiwle R, Sanghi DK. An Update: On Needle Free Injections. IJPCBS., 2014; 4(1):129-138.

[9] Mohanty C. Needle free drug delivery systems. International Journal of Pharmaceutical Research and Development 2011; 3(7): 7-15.

[10] Gibbs S. Needle free insulin devices- how does it work? British Journal of Diabetes and Vascular Disease. 2004; 4 (2): 2004,

[12] Vishnu P, Sandhya M, Sreesh Kiran R, Vani V, Babu NK. Needle Free Injection Technology: A Review. International Journal of Pharmacy 2012; 2(1): 148-155.

[13] United States Patent (needle free injection system)Patent No: US6,676,630 B2

[14] Burkoth TL, Bellhouse BJ, Hewson G, Longridge DJ, Muddle AG, Sarphie DF. Transdermal and transmucosal powdered drug delivery. Crit. Rev. Ther. Drug Carrier Syst. 1999; 16: 331–84

[15] Reddy MS, Kumar MR, Kumar SK, Goli A, Kumar PS. Review on Needle free drug delivery systems. International Journal of Review in Life Sciences 2011; 1(2): 76-82

[16] Kolhe S, Sontakke S. A Review on needle free drug delivery system. International journal of current pharmaceutical research. 2013; 5(2): 66.

[17] Potter C. Caretek medical device. Management Forum Conference on Needle-Free Injection Systems and Auto- Injectors. Management Forum, London, England, Feb 23, 2004.

[18] Baxter J, Mitragotri S. Needle-free jet injections: dependence of jet penetration and dispersion in the skin on jet power. Journal of Control Release. 2004; 97(3): 527-535.

[19] Donnelly R, Singh R, Woolfson D. Micro needle-based drug delivery systems: Micro fabrication drug delivery and safety. Drug delivery journal 2010; 17(4): 187-207

[20] www.prnewswire.com/news-releases/aradigm-acquires-intrajectr-needle-freetechnology-from-weston-medical-55667032.html.

[21] A future free from needles. World Pharmaceutical Frontiers; www.worldpharmaceuticals.net, Page no. 20-22.