WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 7.523
Volume 7, Issue 2, 393-403. Review Article ISSN 2277– 7105

A REVIEW ON NEEDLE-FREE INJECTION TECHNOLOGY

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Article Received on
30 Nov. 2017,
Revised on 21 Dec. 2017,
Accepted on 11 Jan. 2018
DOI: 10.20959/wjpr20182-10736

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ABSTRACT

Needle free injection system in a novel method for the introduction of medication into patients. It reduces the patient concern about the use of needles. It is effective for delivering a wide range of drugs and are found to be bioequivalent to that of the conventional needle and syringe. Not only it can benefit the pharmaceutical industry in increasing product sales, it has the added potential to increase compliance with various dosage regimens and improved outcomes. Today, they are emerging as a novel technology that promises to make the administration of medicine more efficient and less painful.

KEYWORDS: Needle free injection system efficient and less painful.

INTRODUCTION

Needle-free injection system is a novel method for the introduction of drug into patients. Instead of creating a puncture on the skin surface needle-free injection devices forces the medication through skin pores by the help of air pressure, thereby effectively delivering the drug without the use of needles. First air powered needle-free injection devices were developed during 1940s for the mass administration of vaccine to the US soldiers. Needle injection is the one of the most invasive method of drug administration which damages the tissue which may not heal properly in case of patients suffering from diabetes and in case of careless injection, a patient can die from administering tiny bubbles of air into the vein, infection or inflammation. Needles although effective possess several drawbacks: they are painful, expensive, lacks reusability etc. Needle-free systems are designed to overcome these problems making them safer, less expensive and more convenient. This technology is being backed by World Health Organization and various groups including Bill and Melinda Gates Foundation. This technology find it highly useful in mass immunization programs, bypassing

the chances of needle stick injuries and avoiding other complications arising due to multiple use of single needle without proper sterilization.

PRINCIPLE

NFIT uses the energy which is stronger enough to propel a premeasured dose of medication, loaded in specific unique "cassettes" which can be rigged with the system. These forces can be generated from any of the ways ranging from high-pressure fluids including gases, electro-magnetic forces, shock waves or any form of energy that is capable enough to impart a motion to the medicament.

CLASSIFICATION

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 site of delivery**

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

1. ON THE BASIS OF WORKING

Spring system

Springs have been used to store energy and they were found to be quite effective in powering NFIT devices. The storage of energy and further transmittance via spring is one of the easiest and simplest and the design of the spring must follow the standard protocols. In spring

assisted NFIT, the pressure shall gradually decreases throughout the injection in accordance with the Hook's law and it is one of the drawback of spring powered NFITs.

Laser powered

Laser powered NFI system blasts microscopic jets of drugs into the skin. This technology uses an erbium-doped yttrium garnet laser (which is used in the care of laser resurfacing of the skin) to drive a very fine and precise stream of medicament into the skin with the right amount of force. The device consists of an adapter to hold the drug to be administered and also contains a chamber for water which is used to drive the medicine and is separated from the medicament with the help of a membrane.

Energy propelled system

The force required to propel the drug in order to have a penetrating effect on the skin can also be generated by using energy in various forms.

Lorentz force

The main component of the device which uses the Lorentz force is the actuator which facilitates the entire process. It consists of a small and powerful magnet, surrounded by a wire coil that remains attached to a piston which is inside a drug ampoule. When current is applied, it interacts with the magnetic field and produce a force that pushes the attached piston forward, and the forces a thin stream of the medication from the device. This type of NFIT are system suitable for corneal drug application and for paediatric use.

Gas propelled/air forced

They are also known as jet injectors. They can be used for delivering large volume of medicaments. They are commonly employed for mass vaccination and can deliver the drug to the various tissue depths. The commonly used gases include nitrogen carbon dioxide, helium etc. The major drawbacks associated with this technology are the complicated validation protocols, foul odour due to combustion of reactants etc.

Shock waves

Shock waves are generated by a sudden release of energy and this can be utilised to target the medication to the required site. A micro-blast is induced and it propagates at supersonic speed, yielding high pressure and temperature. The pressure generated is strong and potent so

as to eject the drug and penetrate the skin without affecting the integrity of the skin and underlying tissues.

2. ON THE BASIS OF TYPE OF LOAD

Liquid NFI

It is the first variant of NFI system. The mechanism of achieving a successful injection by needle free injection system depends upon the ability to produce a liquid jet that is stronger enough to penetrate the skin without damaging the skin and properties of the medicament. In this system the orifice of the device is placed exactly over the skin surface and the fluid is forced at an optimum pressure to keep the holes open and pressure should be sufficient enough to prevent the resealing of the hole. The pressure drops quickly so that it does not damage the underling tissues.

Powder NFI

In powder needle-free injection system a premeasured dose of powder medication is put into the drug cascade which is then opened by the means of compressed air and thus medication is delivered to the tissue. The powders used in this system should have specific properties and specific size to ensure their spreading in tissues. In this system the particle exist from the nozzle along with the gas stream and impinges on the skin surface. The powder gets deposited into the hole in a spherical pattern and spread across the stratus corneum. This method is more advantageous over other method as the therapeutic agent will be more stable and does not require process like cold storage. This method is suitable for DNA vaccines and local anaesthetics. Drug delivery through this system is limited only to those medications whose effective dose is about 1 mg max.

Projectile/depot NFI

It is a highly advanced method when compared to the other variants of the NFITs, the drug is processed into a long thin depot having sufficient mechanical strength and are given to the muscle where they create a store of drug which is then released continuously for a specific period of time. It is suitable for therapeutic agents like proteins antibiotics and other smaller molecules.

3. ON THE BASIS OF SITE OF DELIVERY

Intradermal injector

These systems have been used to deliver DNA-based vaccines to the intradermal layer i.e between the layers of the skin.

Intramuscular injector

The delivery of drug through this system is the deepest among all. This system is commonly used for the delivery of vaccines.

Subcutaneous injector

In this system medicament is delivered to the adipose layer just below the skin. This can be used for the delivery of therapeutic proteins like growth hormones to the subcutaneous depth.

MANUFACTURING OF NEEDLE FREE INJECTION TECHNOLOGY

There are a number of ways for manufacturing the NFIT devices; however, the following discussion gives an insight over the production of an air forced system.

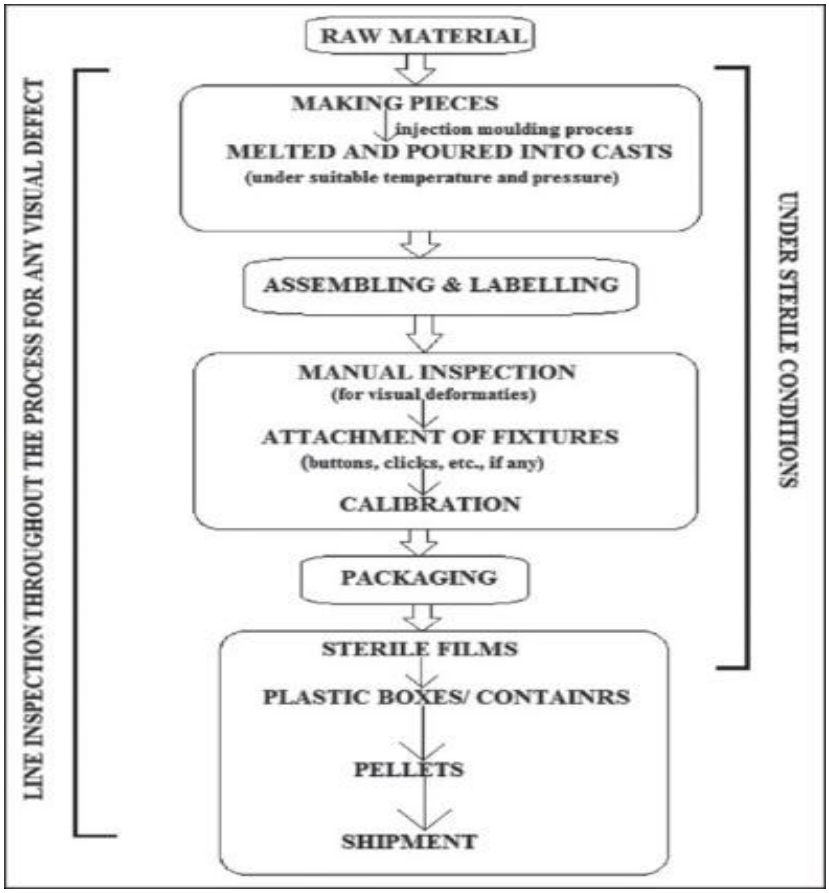

Figure 1: steps involved in the manufacturing of NFI.

As the device is in direct contact with the skin surface, it should be made from materials that are pharmacologically inert. Synthetically produced polycarbonates including thermoplastics are easier to mould and they are light in weight. This makes them the most suitable raw material for the preparation of outer compartment of NFI. Colorants are added if needed. The body of device is made such that it does not react with gases or other gents used in the preparation.

An extremely versatile process of plastic manufacturing called **injection moulding process** is used in the preparation of needle-free injection device. I this method the raw materials are made into pellets and are fed in to the hopper by either manual or mechanical method. Then the pellets are directed into the cylindrical body of the machine with the help of a rotating screw. The pellets are then melt due to frictional forces generated by the gliding of pellets over one another and the tube may be heated externally to increase the temperature to aid the process.

The melt is then introduced into the mold and it is kept for some time under increased pressure and then they are allowed to cool and harden. The mold parts are then opened and eject the formed design. It is then checked for deformities.

It is then transported into the assembly line where markings are applied on its parts. These markings include those for dose level etc. any attachments like buttons are fixed in this stage. The devices are then first wrapped in sterile films and then put into cardboard or plastic boxes.

The entire process is supervised by line inspectors for any visual defects and structural deformity. The device is also checked for accuracy and precision. These devices are manufactured under strict control of FDA and FDA conducts inspection of the manufacturing unit at regular intervals.

COMMERCIALLY AVAILABLE NEEDLE-FREE INJECTION DEVICES

Device name	Energy source	Maximum volume (in ml)	Comments
Biojector 2000	Gas propelled (CO_2)	Up to 1	Able to deliver intra-muscular, subcutaneous and intra-dermal injection
Vitajet 3	Spring powered	0.5	For subcutaneous administration only
Tev-Tropin®	Spring powered	Variable (as directed by physician)	For subcutaneous administration only
Sumavel®DosePro™	Gas propelled (compressed nitrogen gas)	0.5	For subcutaneous administration only, prefilled single unit
Bioject®ZetaJet™	Spring powered	0.05-0.5	Highly efficient for mass immunization, self-medication, can deliver intra-muscular, subcutaneous or intra-dermal
PharmaJet Stratis®	Spring powered	0.5	Penetrate skin in about one tenth of second. No external power required
Jupiter Jet™	Gas propelled (CO_2) (either by gas cartridge or an external CO_2 tank)	0.03-0.2 ml, prefilled variants of 3, 5, 10 available	Deliver intra-muscular, subcutaneous or intra-dermal. Efficient in delivering extremely low doses
ChemLock™	Gas generated	Variable (as directed by physician)	First needle free closed system transfer device to receive FDA 510 (K) clearance

Source:bioject.com; pharmajet.com/product/. FDA: Food and drug administrations

Figure 2: Commercially available NFI devices.

ADVANTAGES

- Eliminates needle phobia
- Increases patient compliance and vaccination rate
- It is trouble free, simple and self-administered.
- Solid pellets can also be administered
- Lower pain and stress.
- Minimal skin response and no bleeding or bruising.

DISADVANTAGES

- High start-up cost.
- Greater complexity.
- Cannot be used for Intravenous route.
- Infrastructure for exhaustible gas systems.
- Higher requirement for training and maintenance

APPLICATIONS

- It can be used for the intramuscular, subcutaneous and intradermal **administration of vaccines** like small pox and measles vaccine.
- It can be used for the intradermal **administration of hormones** like growth hormones.
- It can be used for the intradermal **administration of anaesthetics** like local anaesthetics.
- It can be used for the subcutaneous **administration of insulin**.

- It can be used in the **treatment of migraine** like for the administration of drugs like sumatriptan.

CONCLUSION

Needle free technology are capable of delivering a wide spectrum of medicinal formulations into the body with the same bioequivalence as that of drug administration by a two-piece syringe system, without inflating unnecessary pain to the patients. These are very easy to use, doesn't require any expert supervision or handling, easy to store and dispose. They can even deliver the drug to the most sensitive parts of the body like cornea. They are efficient to administer the medication to intra-muscular, subcutaneous and intra-dermal layers of the skin. Most of the needle-free injection system are still in the developing stage. Researches are also being carried out to make them more user friendly, painless and to administer more dosage forms. If the current trend continuous, this system can be effectively implemented for increasing the vaccination rate in developing countries. To achieve this objective the initiation should be taken up by the multinational companies otherwise it will remain as a dream.

REFERENCE

1. Patwekar SL, Gattani SG, Pande MM. Needle free injection system: A review. Int J Pharm Sci., 2013; 5: 14–9.
2. Kale TR, Momin M. Needle free injection technology - An overview. [Last cited on 2014 Oct 12]; Innov Pharm, 2014; 5: 1–8.
3. Vishnu P, Sandhya M, Sreesh Kiran R, Vani ChV, Naveen Babu K. Needle Free Injection Technology: A review. Int J Pharm., 2012; 2: 148–55.
4. Chavan B, Doshi A, Malode Y, Misal B. Review on needle free drug delivery systems. Int J Pharm Res Rev., 2013; 2: 30–36.
5. Kumar RB. Needle free injection systems. Pharma Innov, 2012; 1: 57–72.
6. Kumar RM, Reddy SM, Kumar SK, Goli A, Kumar SP. Review on needle free drug delivery systems. Int J Rev Life Sci., 2011; 1: 76–82.
7. Garg T. An evolutionary approachs in development of needle free injection technologies. Int J Pharm Pharm Sci., 2012; 4(Suppl 1).
8. Kohle S, Sontake S. A review on needle free drug delivery system. Int J Pharm Pharm Sci., 2013; 5: 15–20.

9. Ren T, Wang X, Yang PH. Vaccine and Needle free vaccination delivery system. J Microb Biochem Technol, 2014; 6: 359–60.
10. King T. Encyclopedia of Pharmaceutical Technology. 3rd ed. Vol. I. James Swarbrick Informa Healthcare; 2007. Drug delivery: Needle-free systems, 1212.
11. Yoh J. Er:YAG laser pulse for small-dose splashback-free microjet transdermal drug delivery. [Last updated on 2012 Sep 13; Last cited on 2014 Dec 18];Opt Lett. 2012 37:3894–6. Available from: http://www.osa.org/en-us/about_osa/newsroom/news_releases/2012/laser-powered_%E2%80%98needle%E2%80%99_promises_pain-free_injectio/ [PubMed]
12. Hunter I, George N. Vaccines and injections soon to be delivered via small needleless high-pressure jets. J Med Eng Phys. 2012. [Last updated on 2012 May 26; Last cited on 2014 Dec 18]. Available from: http://therefusers.com/refusers-newsroom/vaccines-to-be-delivered-via-small-needleless-high-pressurejets-preventdisease-com.
13. King T. The Challenges in Commercialisation of a Needle-Free Device. Management Forum Conference -Needle-Free Injection Systems and Auto-Injectors; February 26, 2002; London, England.
14. Jagadeesh G, Prakash GD, Rakesh SG, et al. Needleless Vaccine Delivery Using Micro-Shock Waves. Clinical and Vaccine Immunology: CVI, 2011; 18: 539–45. [PMC free article] [PubMed]
15. Shergold OA. The Mechanics of Needle-Free Injection Ph.D. Thesis, University of Cambridge. Cambridge, England: 2004.
16. Baker AB, Sanders JE. Fluid mechanics analysis of a spring-loaded jet injector. IEEE Trans Biomed Eng, 1999; 46: 235–42. [PubMed]
17. Schramm J, Mitragotri S. Transdermal drug delivery by jet injectors: Energetics of jet formation and penetration. Pharm Res., 2002; 19: 1673–9. [PubMed]
18. 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. [PubMed]
19. Dégano P, Sarphie DF, Bangham CR. Intradermal DNA immunization of mice against influenza A virus using the novel PowderJect system. Vaccine, 1998; 16: 394–8. [PubMed]
20. Duckworth GM, Millward HR, Potter CD, Hewson G, Burkoth TL, Bellhouse BJ. Oral PowderJect: A novel system for administering local anaesthetic to the oral mucosa. Br Dent J., 1998; 185: 536–9. [PubMed]

21. Potter C. Caretek Medical Device. Management Forum Conference on Needle-Free Injection Systems and Auto-Injectors. Management Forum; February 23, 2004; London, England.
22. Herndon TO, Gonzalez S, Gowrishankar TR, Anderson RR, Weaver JC. Transdermal microconduits by microscission for drug delivery and sample acquisition. BMC Med., 2004; 2: 12. [PMC free article] [PubMed]
23. Glenn GM, Flyer DC, Ellingsworth LR, Frech SA, Frerichs DM, Seid RC, et al. Transcutaneous immunization with heat-labile enterotoxin: Development of a needle-free vaccine patch. Expert Rev Vaccines, 2007; 6: 809–19.[PubMed]
24. Prausnitz MR, Langer R. Transdermal drug delivery. [Last updated on 2009 Jun 23; Last cited on 2014 Dec 24];Nat Biotechnol, 2008; 26: 1261–8. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2700785/[PMC free article] [PubMed]
25. Daddona P. Transdermal technology: Macroflux transdermal technology development for the delivery of therapeutic peptides & proteins. Drug Deliv Technol, 2002; 2: 54–7.
26. Pray WS, Pray JJ. Blood glucose meters: A dynamic market. US Pharm, 2002; 27: 18–23.
27. Cygnus, Inc. Sankyo Pharma and Cygnus Announce FDA Approval for Pediatric Use of GlucoWatch G2 Biographer. [Last updated on 2003 Mar 03; Last cited on 2014 Dec 24]. Available from: http://www.cygn.com/press/082802.html.
28. Statland BE. GlucoWatch Automatic Glucose Biographer. [Last updated on 2002 Aug 28; Last cited on 2014 Dec 24]. Available from: http://www.fda.gov/cdrh/pdf/P990026a.pdf.
29. Sarah CP. Under the Skin of Intra-Dermal Vaccines, Proceedings of the National Academy of Sciences; Published on June 18, 2013; 10049–51. [PMC free article] [PubMed]
30. Richard T. Skin Delivery of Biological, Transdermal Patches, Microneedles and Needle-Free Injections: Manufacturing Lines Roll as Concepts Become Products. On Drug Delivery. 2013. Mar-Apr. Available at: http://www.ondrugdelivery.com/publications/Transdermal_Microneedles_NFI_March_2013/Transdermal_Microneedles_NFI_March_2013_Low_Res.pdf.
31. Bioject Needle Free Injection Technology, Bioject Medical Technologies Inc., Leader in the Development of Needle-Free Injection Therapies. [Last updated on 2014 Oct 20; Last cited on 2014 Dec 18]. Available from: http://www.bioject.com/technology.
32. Zogenix.com, where Medicines Meet Technology. [Last updated on 2012 Oct 14; Last cited on 2014 Dec 24]. Available from: http://www.zogenix.com/content/technology/dosepro.htm.

33. King T. “Intraject”. Management Forum Conference on “Needle-Free Injection Systems and Auto-Injectors”. Management Forum; February 23, 2004; London, England.
34. King T. Encyclopedia of Pharmaceutical Technology-Viscosity. 3rd ed. James Swarbrick Informa Healthcare; Drug delivery: Needle-free systems, 2007; I: 1214.
35. Garg T. An evolutionary approachs in development of needle free injection technologies. Int J Pharm Pharm Sci., 2012; 4(1): 590–6.
36. Sanghi DK, Tiwle R. An Update: On needle free injections. Int J Pharm Chem Biol Sci., 2014; 4: 129–38.
37. Waghmare PV. A Review on Needle-Free Injection Systems: Novel Approach to Drug Delivery. PHARMATUTOR-ART-1888. [Last updated on 2013 Feb 03; Last cited on 2014 Dec 26]. Available from: http://www.pharmatutor.org/articles/review-on-needle-freeinjection-systems-novel-approach-drug-delivery?page=0,0.