Review Article

www.ijrap.net (ISSN:2229–3566)

NEEDLE FREE INJECTION TECHNOLOGY: A REVIEW

Geetha Pushpanjali S [1], Leela Praveena V [1], Swamy P V [2]*

[1] Department of Pharmaceutical Quality Assurance, Shri Vishnu College of Pharmacy, Bhimavaram, West Godavari District, Andhra Pradesh, India

[2] Department of Pharmaceutics, Shri Vishnu College of Pharmacy, Bhimavaram, West Godavari District, Andhra Pradesh, India

Received on: 15/07/20 Accepted on: 15/08/20

***Corresponding author**
E-mail: vspadavala@svcp.edu.in

DOI: 10.7897/2277-4343.1105170

ABSTRACT

Needleless injection systems are novel ways to introduce various medicines into patients without piercing a conventional needle. Needleless injection technology was developed to reduce the number of needle-stick accidents and associated problems; easy to use, disposable and their use is expected to increase considerably. Self-administration is feasible with these devices. This technology is used to deliver not only drugs but also proteins, peptides, monoclonal antibodies, small molecules and vaccines. This review describes pre-requisites, comparison between hypodermic and needle free injections, manufacturing process, components, types and marketed products.

Keywords: Needle-free injections, Needle-free technology, Needle-free devices, drug administration and drug delivery.

INTRODUCTION

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 re-used 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. These technologies are meant for injecting liquid formulations, as well as injecting drugs and vaccines in a solid particle dosage form.[1,2]

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.

History

The first hypodermic syringes were developed by French surgeon, Charles Gabriel Pravaz, in 1853, although there is a minor development in syringes since then, the technology has remained unchanged for the last 150 years. Needle-free drug delivery was first described in the early 20th century by Marshall Lockhart in 1936 in his patent jet injection.[3] Then in the early 1940s 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.

Structure of Human Skin

The knowledge of the structure of the skin is essential to the successful administration of drugs through the needle-free injection systems as these drugs are administered to the skin. Human skin is generally made of two layers: Epidermis and Dermis.[4,5]

The epidermis

Epidermal layer acts as a physical and chemical barrier between the body and external environment. This is a stratified squamous epithelium layer, i.e., is composed primarily of two types of cells: keratinocytes and dendritic cells.

The Epidermis harbours a number of other cells such as melanocytes, Langerhans cells and Merkel cells. But the keratinocyte type cells comprise the majority of the cells by far.

The layers of epidermis are:

Stratum germinativum: It contains column-shaped keratinocytes that attach to the basement membrane zone with their long axis perpendicular to the dermis.

Stratum spinosum: Its thickness varies from 5-10 cells. Intercellular spaces between spinous cells are bridged by abundant desmosomes (adhering spots) that promote coupling between cells of the epidermis and provide resistance to physical stresses.

Stratum granulosum: It contains living cells; these are responsible for further synthesis and modification of proteins involved in keratinisation. It is 1-3 cells layer in thickness.

Stratum corneum: In this layer the cells are rich in protein and low in lipid content (hydrophilic nature); are surrounded by a continuous extracellular lipid matrix.

Malpighian layer

In this layer, protoplasm has not yet changed into horny material.

The dermal-epidermal layer

It acts as a support for the epidermis, establishes cell polarity and direction of growth, directs the organization of the cytoskeleton in basal cells; provides developmental signals and function as a semi-permeable barrier between layers.

The dermis

It is an integrated system of fibrous, filamentous and amorphous connective tissue that accommodates stimulus-induced entry by nerve, vascular-networks, appendages, fibroblasts and mast cells. Its thickness ranges from 2000-3000 μm. The principal component of the dermis is collagen and represents 70% of the skin's dry weight. Its main function is to protect the body from stress and strain. A sense of touch and heat is provided by the mechanoreceptors harboured by the dermis.

Subcutaneous Tissue (Connective Tissue)

The subcutaneous tissue or hypodermis is not actually considered a true part of the structured connective tissue which is composed of loose textured, white, fibrous connective tissue containing blood and lymph vessels. This layer regulates the drug permeation through the skin to enter the circulatory system before reaching the hypodermis, although the fatty tissue could serve as a depot of the drug.

Pre-requisites

Shelf-life

Needle type injection systems are having longer shelf-life. The mechanics of the device must be to enable it being trigged even after 2-3 years of storage in varied storage conditions.

While manufacturing the needle-free injection systems, the following points need to be considered over the entirely intended shelf-life: The product must remain sterile throughout its shelf-life; endotoxins and foreign particulates must not exceed the predetermined limit; the leachable profile into the formulation from the contact component of the device must not be excessive, rather acceptable; the purity, composition and concentration shall not be compromised throughout the intended shelf-life in any case; the entire device must be made of a material which remains stable, offer good mechanical strength, cost effective and inert in nature.[6]

Viscosity

As the viscosity of the formulation increases, force required to deliver the drug also increases.[7] Needle-free systems are formulated with varying viscosities which helps in easy drug delivery for different formulations

Advantages of needle-free drug delivery

The following are the advantages of needle-free injection systems: They eliminate needle phobia for patients; eliminate the risk of broken needles; reduced costs; promote patient compliance; reduced vaccine volume; low pain and stress; targeted immune response; fewer injection site lesions; consistent vaccine delivery; excellent dose response; eliminate cross-contamination; excellent dose-response with increased drug doses; bio-equivalence has been demonstrated enabling the development of generic drug proteins; provide rapid delivery and reproducibility comparable with needle and syringe; improved bioavailability over other non- or less invasive drug delivery systems; improved immune response to DNA and conventional vaccines; provide the capability to alter the pharmacokinetics of certain drugs.[8]

Newest Needle-Free Injection System

The Needle-free injection system represents the latest alternative to injection on the market and can deliver transdermally ionic drug solution into the body for medical purposes. It has the capability of transdermal delivery of ionic solution of drugs for the first time ever of either micro or macromolecules (greater than 800, 000 Daltons). When drugs are delivered by NFI system, there are no chances of electrolysis of ionic drug solutions or variation in pH of the ionic drug solutions. Both positive and negative ions of the drug are transdermally delivered at the same time. Patient's perception of electrical pulses is decreased due to vibration feature; it is non-invasive in action and hence, there is no trauma from injections.

The comparative aspects of hypodermic injections and needle-free injection systems (NFI systems) are represented in Table 1 and depicted in Figure 1.

Raw Materials

These devices are fabricated from pharmacologically inert materials as they are directly coming in contact with the body. The materials can withstand higher temperature since they are heat sterilized. Air-forced injection devices are available in different shapes and sizes.[9]

The raw materials which are required for manufacturing process are:

Thermoplastic material

The external body of the device is made up of a thermoplastic material which has characteristics such as high strength and lightweight. Example: Polycarbonate.

Fillers

The fillers are added which make plastics more durable, lightweight and rigid.

Colorants

Colorants are added to modify the elegance. Before manufacturing, the plastics are typically supplied in pellet form with the colorants and fillers already incorporated. Air-forced systems mainly use carbon dioxide or Helium gas to propel the drug into the body.

Design

Following are the three components from which the air-forced needle-free injection systems are typically made; these are: injection device, a disposable needle-free syringe and an air cartridge.

The injection device is made of a durable plastic. It is designed to hold the drug for self-administration.

The needle-free syringe is also plastic. It is sterilized because it comes in contact with the skin. A disposable syringe is used every time. The portable units include pressurized metal air cartridges. Some of these types of devices are having air hook-ups, which help to attach the larger containers of compressed air.

To generate the pushing force instead of pressurized air cartridges a re-usable spring is used by some air-forced systems.

Manufacturing Process

There are several methods for manufacturing the needle-free injection system. Here the process focuses on the production of an air-forced system.[10,14]

These systems are made through the following procedure which involves molding the pieces, assembling them, decorating and labeling.

Typically, the individual pieces are produced off-site and assembled by the needle-free injection system manufacturer. To prevent the spread of disease all the manufacturing processes are done under sterile condition.[11-13]

Molding

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.

Assembling and labeling

The next process is to assemble the pieces and transport the parts to an assembly line. Various events occur during this production phase. Each printing is made by these machines and is so precise because these machines are specially calibrated. Depending on the complexity of the device, either manually or with the assistance of machinery, the devices are assembled. This involves inserting the various pieces into the main housing and attaching any buttons.[15]

Packaging

The next step after the assembling process is packaging. The systems are wrapped in sterile films before packed into card-board boxes or plastic boxes. Packing of each part reduces the movement, which prevents damage. An instruction manual (includes safety information) is provided for consumer products. Then these boxes are stacked on pallets and shipped via truck to distributors.

Quality Control

Quality control checks are performed throughout the manufacturing process. Checking of the plastic components is done by line inspectors to assure that the needle-free injection devices confirm all the predetermined specifications. The first test method is visual inspections, but to check the dimensions (size and thickness) the measuring equipment is also used; instruments like laser micrometers, calipers and microscopes are used. Inspectors also check to make sure the printing and labeling is correct and that all the parts are included in the final packages. Each manufacturer must conform to various production standards and specifications. Detailed records related to production and design must be kept because announced and unannounced inspections may occur to ensure that these companies are following good manufacturing practices.[15]

Components of Needle-Free Injection Device

Needle-free injection device (Figure 2) consists of 3 main components:[16]

Component 1- Injection device

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

Component 2-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 releases drug particles at a typical speed of 100 m/s with a depth of 2 mm. The most common orifice size is 0.127 mm, comparable to a 25-gauge needle. Thus, this injection is painless, the patient feels tap of gas on the skin which is like flicking your finger against your skin.

Component 3-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 has a pressure storage method that utilizes compressed gas in gas-cartridge. The most popular gases used in devices are carbon dioxide or nitrogen. Pressurized metal air cartridges are often provided for access in portable units. The precision of drug delivery and stress imposed on the product is influenced by device design. The device must assure the generation of sufficient high pressure to cause skin puncture as well as not harming the drug molecule. Fragile drug molecules are susceptible to damage due to high pressure (e.g., monoclonal antibodies). Hence, devices may vary in design depending upon the drug for which they are used.[17-20]

Classification of Needle-Free Injection Technology

On the basis of working, NFI systems are categorized as: Spring, laser-powered, energy propelled, Lorentz force actuator, shockwave assisted and gas-propelled/air-forced systems.[21-23]

On the basis of the type of load, they can be classified as liquid, powder and projectile systems. On the basis of the mechanism of drug delivery, they are classified as nano-patches, sandpaper assisted delivery, iontophoresis enabled systems and micro-needle patches. On the basis of site of delivery; they can be grouped as intradermal injectors, intramuscular injectors and subcutaneous injectors.

Classification on the basis of working

Spring systems

Springs have been proven to be quite effective in powering needle-free injection technology devices as it involves in energy storage and further transmittance via spring which is one of the easiest and simplest methods.

The basic problem with this type of systems is that the force provided by springs will reduce in portion with respect to distance over which the load has been applied and will reduce the elasticity of the spring on prolonged usage of the device.[24]

Laser-powdered systems

The technology utilizes an erbium-doped Yttriumgarnet laser to drive a very fine and precise stream of drug or medicament with the right amount of force.

It contains two chambers: The laser is integrated with an adapter to hold the drug that is to be administered. It also contains a chamber for water, which helps to drive the medicine.

Energy propelled systems

The various forms of energy generated should be used to propel the drug so as to have penetration effect.

Lorentz force actuator systems

The main component of this device is Lorentz force actuator which facilitates to push the piston forward ejecting the drug at a very high pressure and velocity to that of sound in air[24].

Gas propelled/air-forced systems

They may be either for single use or need a periodic replacement of the gas cartridge. Some devices employ gas as a simple spring where the stored gas accelerates the piston; they are portable and compact; however, developing a gas spring retains a specific proportion of the gas to work at the lapse of its shelf-life.

This type of system offers greater scope as it offers higher energy density than metal spring and allows the combustion of the gas to power the device.[25]

Shockwave assisted systems

Shockwaves are generated by any sudden release of energy. These disturbances carry energy and can be propagated through a medium. The major energy prototype may be an ignition system or a source of explosive materials.[26]

Classification on the basis of the type of load

Liquid based systems

The basic principle involved is the ability of the liquid jet that is stronger enough to penetrate the skin and underlying fat layer without harming the skin, thereby delivering of the drug under administration. The mechanism in delivery of the drug was high enough pressure generated by a fluid in intimate contact with the skin and then the liquid will punch a hole in to the skin and be delivered in to the tissues in and under the skin. The device has sufficient pressure to the skin.

Delivering fluid from NFI system involves a thorough application of fluid mechanics. The steps involved are: Registration-the orifice of the device is placed exactly over the pores of the skin; exact pressure- the fluid must be forced at an optimum pressure, stronger enough that it keeps the holes in the skin open and consistent enough that it avoids the resealing of the holes; channel drilling-the initial pulse of the fluid drill a channel into the fat layer deep enough that the dose is drifted from the hole into the skin; quicker pressure fall- the pressure drops quickly and sufficiently so that the fluid may not penetrate the muscles underlying the skin.[27-29]

Powder injections

The basic principle involves the usage of non-reactive gas Helium to formulate the particles of sufficient density and accelerating them to sufficient velocity string enough to penetrate into the skin to achieve therapeutic dose levels.[29] The vector or medium should be used to carry or coat the particles.

Depot or projectile systems

Depot injections are given in the muscle where they create a store of a drug which is released continuously over a specified period of time, as the depot will be formulated in a manner to have sufficient mechanical strength that is strong enough to transmit the drug under administration.[30]

Classification on the basis of the mechanism of drug delivery

Nano-patches

The working of nano-patch or micro-projection depends on the use of an applicator to deliver the drug through the skin via the nano-patch projections which are invisible to the naked eye. Nano-patches enable the vaccine to reach the key immune cells located below the skin surface while the entire process is pain-free.

Sandpaper assisted delivery

As "sand-paper" kind of agent is rubbed onto the skin so as to result in micro-derma abrasion phenomena where the superficial layer of the skin is removed, thereby facilitating the entire drug delivery process.[31] Micro-derma abrasion has been widely accepted for cosmetic purposes. Sand-paper aided drug delivery has been successful in increasing the skin permeability, for several vaccines and other methods of micro-derma abrasion have been used to facilitate the movement of drugs such as lidocaine and 5-flurouracil.

Iontophoresis enabled delivery

The lipophilic nature of skin debars several salts and other molecules from entering the skin. In iontophoresis, a small electric current of approximately 0.5 mA/cm^2 is used to force several drug molecules across the skin. The working of this method involves the use of two electrodes as patches, where one acts as a drug reservoir, which can either be positively or negatively charged depending upon the nature of the drug, another patch is placed somewhere else on the body to complete the circuit.

Micro-needle patches

Micro-needle patches, as the name suggests, employ thousands of tiny spikes all around 750 µm long so as to deliver the drug into the skin, while the piercing is not deep enough to hit the blood vessels or even the pain receptors so as to cause pain; hence show better patient compliance.[32]

Classification on the basis of site of delivery

Intradermal injector

These systems are majorly involved in delivery of comparatively newer, DNA-based vaccines to the intra-dermal layer and delivers the drug at a very shallow depth, that is, between the layers of the skin

Intramuscular injector

Drug delivery via this system is the deepest among all and majorly used for vaccination.

Subcutaneous injector

These systems are majorly involved in delivery of human growth hormones due to ease of administration of required dosage unit into the adipose layer just below the skin.

Mechanism of Working

Needle-free injection technology works by forcing the drug at high speed through a tiny orifice that is held against the skin. Needle-free injection technology utilizes force generated by a compressed gas, i.e., air, carbon dioxide (CO_2) or nitrogen (N_2) to propel the drug at high velocity through small orifice (Figure 3). This facilitates an ultra-fine stream of high-pressure fluid that penetrates the skin without using a needle.

When administered through the skin, an ultra-fine stream of fluid penetrates the skin, delivering the drug in a fraction of second to the skin, subcutaneous tissue and intramuscular tissue. Injection event requires less than 0.5 seconds.[33,34]

Stages of Delivery

It involves three phases:

Peak pressure phase- in this phase, optimal pressure is used to penetrate the skin; the time required to penetrate the skin is less than 0.025 sec.

Delivery or dispersion phase– It lasts up to 0.2 sec.

Drop-off phase – It lasts for less than 0.05 sec.

The total amount of time required to deliver the drug is up to 0.5 seconds.[17-20]

Applications

Intraject (Weston Medical) Technology is used to deliver drugs including proteins, peptides, monoclonal antibodies, small molecules and vaccines. Medi-Jector vision (Antares Pharma, lnc.) Technology is used to create a micro thin stream of insulin that penetrates the skin. Powderject 17 (Powderject Pharmaceuticals) Technology delivered insulin to hairless guinea pigs, delivery of large macro-molecules across the skin; used for intra-dermal delivery and DNA immunization against influenza virus in mice.

Jet Injectors Technologies deliver proteins such as β-interferon and small organic conventional therapeutic agent such as lidocaine (lignocaine) for local anesthesia.

The MHI -500 needle-free devices are used for insulin therapy; subcutaneous, intramuscular/ intra-dermal administration of vaccines (smallpox, polio or measles); intra-dermal administration of hormones (growth hormone) and anesthetics (lidocaine). Also used for administration of sumatriptan in the treatment of migraine.

MS Pulse-250 system is used for administration of veterinary medicines.

Certain types of medicines work better with needle-free injection systems than other. Insulin can be incorporated into an inhaler system which must be administered daily to diabetics. Lidocaine hydrochloride, a local anesthetic is suitable to be delivered needle-free. Various adjunct ingredients included in these medicines include cyclodextrins, lactose, liposomes, amino acids and water.

Marketed Products of Needle-free injection systems (NFI Systems) along with their modes/ routes of administration are presented in Table 2.

Table 1: Comparison of hypodermic injections and NFI systems

Hypodermic injections	NFI
Pain caused by the introduction of the needle or by the drug itself after its injection	Reduced pain at the site of injection
Needle phobia	Eliminates needle phobia
Needle stick injuries	Eliminates the high number of tissue damages that result when a needle breaks upon insertion into a patient
Training required	Training not required. Self- administration is feasible with these devices
May lead to transferrable infections	Due to lack of needle, chances of infections are less
Difficult to insert the needle to correct depth.	Needle-free injections eliminate the possibility of reusing needles from one patient to another by eliminating the needle all together
Necessity of aspirating a needle to ensure not hitting a blood vessel	
The danger of communicating a specific or contagious disease	

Table 2: Marketed Products of NFI Systems

Product	Use
BIOJECTOR	Intramuscular
VITAJET 3	Used for delivery of insulin subcutaneously
SEROJECT	Used for delivering the Serostism recombinant human growth hormone administered subcutaneously. Used for treatment of HIV associated muscle wasting in adults
MHI 500	Subcutaneous administration of insulin

IJECT	Used for prefilled single use, disposable use for subcutaneous or intramuscular administration.
COOLCLICK	Recombinant human growth hormone via the subcutaneous route.
RECOJECT	Deliver recombinant human insulin
INTRAJECT TECHNOLOGY	Liquid protein formulation
BIOVALVE'S MINI JET TECHNOLOGY	Used for intra-dermal, subcutaneous and intramuscular administration
ANTARES MEDI- JECTOR VISION TECHNOLOGY	Delivering insulin
NEEDLE FREE, AUTO AND PEN INJECTOR	Administration of a single dose
MADAJET	Used in dentistry
BIOJECT- ZETAJECT	Subcutaneous and intramuscular use

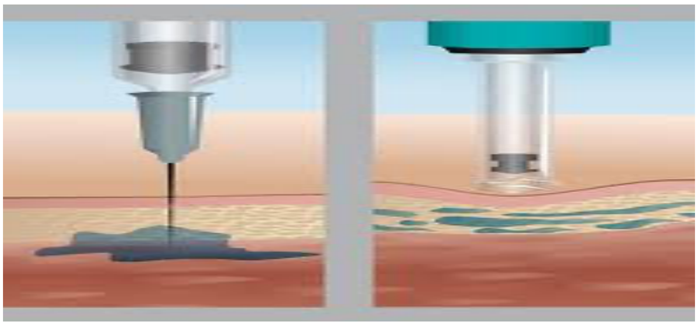

Figure 1: Hypodermic injections Vs needle free injections (courtesy: Shutterstock)

Figure 2: Components of needle-free injection (NFI) system (courtesy: Shutterstock)

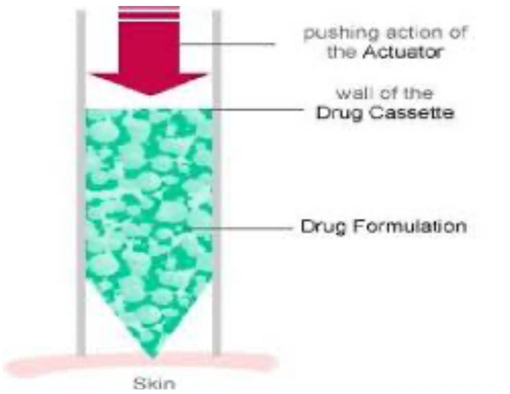

Figure 3: Diagram for Mechanism of working (courtesy: Shutterstock)

CONCLUSION

Finally, due to the pain-less nature of this system, we have long way to improve needle-free injectors which are more patient compliant. Needle-less technology has the best alternative to deliver the medicament into the skin without having any pain. Other benefits include very fast injection compared with conventional needles and no needle disposal issues. Companies are still working on producing devices that are harmless, safer and easier to use.

Future perspective

In the developing world, there are major challenges of disease transmission through re-use of needles. Organizations such as WHO and CDC (Centre for Disease Control) and groups like Bill and Melinda Gates Foundation have supported the development of needle-free alternatives for drug delivery.

There appears to be tremendous opportunity for needle-free technology to have major impact in pharmaceutical industry. 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.

REFERENCES

1. Gupta MM, Vinesh Kumar, Pawan Kumar B. Needle Free Injection: An Alternate Approach of Injection. The Pharma Review 2008; 31(62): 37-41.
2. Smita K, Sneha S. A Review on Needle-Free Drug Delivery System. Int J Curr Pharm Res 2013; 2: 30-6.
3. Lockhart, M. Needle-free drug delivery, US Patent No. 69,199, March 16; 1936.
4. Bisset DL. Anatomy and biochemistry of the skin. In: Kydonieus AF, Berner B, editors. Transdermal delivery of drugs.1st ed. Vol.1. Boca Raton (Florida): CRC Press; 1987. p. 29-42.
5. Buxton PK. ABC of Dermatology. 3rded. London: BMJ Publishing Group; 1998. p. 12-5.
6. King T. Intraject. Management Forum Conference on Needle-Free Injection Systems and Auto-Injectors. Management Forum; February 23; London, England; 2004.
7. King T. Drug delivery: Needle-free systems. In: James Swarbrick, editor. Encyclopedia of Pharmaceutical Technology, 3rded. Vol. I. London: Informa Healthcare; 2007. p. 1214.
8. Kale TR, Momin M. Needle-free injection technology - An overview. Inov Pharm 2014; 5(1): 1-8.
9. Mohd TK, Hemant T, Tahrun N. The Needle Free Injection Technology, February, Conference: Young Researcher's Conference at Institute of Chemical Technology, Mumbai, India; 2011.
10. Raghuveer P, Madhuri D, Rajeswari M. A Review on Needle Free Drug Delivery System. World J Pharm Pharm Sci 2016; 5(6): 449-65.
11. Henry C. Special Delivery. Chemical and Engineering News 2000; 78(38): 49-65.
12. Arora A, Prausnitz MR, Mitragotri S. Micro-scale devices for transdermal drug delivery. Int J Pharm 2008; 364: 227-36.
13. Sunitha Reddy M, Ranjith Kumar M, Sanjay Kumar K, Anil G, Santhosh Kumar P. Review on Needle free drug delivery systems. Int J Rev Life Sci 2011; 1(2): 76-82.
14. Ravi AD, Sadhna D, Nagpaal D, Chawla L. Needle free injection technology: A complete insight. Int J Pharm Investing 2015; 5(4): 192–9.
15. Mitragotri S. Current status and future prospects of needle-free liquid jet injectors. Nat Rev Drug Discov 2006; 5: 543–8.
16. Aguiar JC, Hedstrom RC, Rogers WO, Charoenvit Y, Sacci JB, Lanar DE *et al*. Enhancement of the immune response in rabbits to a malaria DNA vaccine by immunization with a needle-free jet device. Vaccine 2000; 20(1-2): 275-80.
17. Chandan M. Needle free drug delivery systems: A review. Int J Pharm Res Dev 2011; 3(7): 7-15.
18. Roger GH. Needle free drug delivery technology. Innov Pharm Tech. p 60-63. Available from: http://iptonline.com/articles/public/AntaresPharma.pdf (accessed on 30th September 2020)
19. Adam L. Advances in disposable needle-free injector technology. Innov Pharm Tech. p. 100-9. Available from: http://www.iptonline.com/articles/public/IPTFIVE100NP.pdf (accessed on 30th September 2020)
20. Al-kaf AGA, Othman AM. A review on needle free injections. Univ J Pharm Res 2017; 2(2): 1-5.
21. Bharath Kumar R. Needle Free Injection Systems. The Pharma Innovation 2012; 1(9): 57-72.
22. Dukare MV, Saudagar RB. Needle-Free Injection System. Int J Curr Pharm Res 2018; 10(2): 17-24.
23. Kolhe S, Sontakke S. A Review on needle free drug delivery system. Int J Curr Pharm Res 2013; 5(2): 20-8.
24. Hunter I, George N. Vaccines and injections soon to be delivered via small needleless high-pressure jets. J Med Eng Phys 2012; 34: 233-48.
25. Sanghi DK, Tiwle R. An Update: On needle free injections. Int J Pharm Chem Biol Sci 2014; 4(1): 129–38.
26. Burkoth T L, Bellhouse B J, Hewson G, Longridge DJ, Muddle AG, Sarphie DF. Transdermal and transmucosal powdered drug delivery. Crit Rev Ther Drug Carrier Syst 1999; 16: 331-84.
27. Jagadeesh G, Prakash GD, Rakesh SG. Needleless vaccine delivery using micro-shock waves. Clin Vaccine Immunol 2011; 18: 539-45.
28. Baker AB, Sanders JE. Fluid mechanics analysis of a springloaded jet injector. IEEE Trans Biomed Eng 1999; 46: 235-42.
29. Schramm J, Mitragotri S. Transdermal drug delivery by jet injectors: Energetic of jet formation and penetration. Pharm Res 2002; 19: 1673-9.
30. Prausnitz MR, Langer R. Transdermal drug delivery. Nat Biotechnol 2008; 26: 1261-8.
31. Eba H, Nina P, Christina S, Julie H, Reginald A, Jeannine S *et al*. Home Use of the Gluco Watch G2 Biographer in Children With Diabetes. Pediatrics 2005; 115 (3): 662-6.
32. Jian Yang, Xinli Liu, Yunzhi Fu, Yujun Song. Recent advances of micro-needles for biomedical applications: drug delivery and beyond. Acta Pharmaceutica Sinica B 2019; 9(3): 469-83.
33. Harry Brown. Needle free insulin. Br J Diabetes Vasc Dis 2004; 4(2): 113–5.
34. King T. Drug delivery: Needle-free systems. In: James Swarbrick, editor. Encyclopedia of Pharmaceutical Technology, 3rd ed. Vol. I. London: Informa Healthcare; 2007. p. 1212.

Cite this article as:

Geetha Pushpanjali *et al*. Needle Free Injection Technology: A Review. Int. J. Res. Ayurveda Pharm. 2020;11(5):205-211 http://dx.doi.org/10.7897/2277-4343.1105170

Source of support: Nil, Conflict of interest: None Declared