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A Review Article On Needle Free Injection Technology

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Abstract: NFIT i.e., Needle-free injection technology is a comprehensive concept that covers an array of drug delivery systems designed to transport medications through the skin without the need for hypodermic needles. These systems utilize different forces, including Lorentz forces, shock waves, gas pressure or electrophoresis, to eliminate the necessity of using needles for drug administration. This method offers benefits not limited to the pharmaceutical sector, the emerging nations also finds it extremely helpful in mass vaccination campaigns by diminishing the likelihood of needle-related injuries and averting additional associated repercussions, such as those brought on by the repeated use of a single needle. Based on how they operate, the kind of load they carry, how drugs are delivered, and where they are delivered, NFIT devices can be categorized. The key considerations for ensuring a reliable, secure, and efficient drug delivery using NFIT are the drug's viscosity, sterility and shelf life of the medication. Another notable advantage of this technology is its capability to deliver highly viscous medication formulations that are challenging to administer using traditional needle and syringe systems, particularly when employing advanced needle-free injection systems. Needle-free injection technology devices are Produced using various techniques; however, the most used method is the injection molding technique. This technology is being offered in a variety of forms, including Vitajet 3, Tev-Tropin, Bioject ZetaJetTM and others. Numerous devices are already on the market as a result of greater investment in its development and FDA approval.

Index Terms - Bioject ZetaJetTM, Needle free injection technology, Molding technique, Tev-Tropin etc**.**

I. Introduction

NFIT i.e., Needle-free injection technology is a versatile idea that includes a wide range of Methods of delivering medications, spanning a variety of systems by utilizing forces such as Lorentz force, electrophoresis, gas pressure or shock waves these technologies facilitate the administration of medications without the need for traditional needle-based injections, directly into the skin. These mechanisms eliminate the need for conventional hypodermic needles. NFIT holds promise for the pharmaceutical industries as well as for the developing world, where it proves hugely advantageous in large-scale immunization programs. It reduces the likelihood of needle puncture accidents and helps prevent issues that can result from the repeated use of single needles. Needle-free injection technology devices can be classified according to their fundamental principles of operation, the force they utilize, the method of drug release, and the specific location for drug administration. To guarantee the dependable, secure, and efficient administration of medication using NFIT, it is essential to take into account the viscosity, sterility and shelf life of the pharmaceutical product.

Advanced NFIT i.e., needle-free injection systems have the capability to deliver extremely viscous drug formulations that are typically unsuitable for traditional needle and syringe methods. This feature enhances the versatility of NFIT technology. Manufacturing NFIT devices can be achieved through various methods, but injection molding is the widely preferred technique. Several NFIT variants are available in the market, including notable options like Bioject, ZetaJet™, Vitajet 3, and Tev-Tropin. Extensive investments have been made in the development of this technology, resulting in numerous devices receiving FDA clearance and a growing global market presence[1,2].

Needle-free Injection Technology Advantages:

1. Prevents skin perforation troubles; doesn't produce Haemorrhaging or contusions.
2. Provides briskly medicine administration and advanced repetition than invasive medicine delivery styles, and so improves the bioavailability in contrast to penetrative methods of medication delivery.
3. Prevents reconstitution issues and shearing goods.
4. Bettered stability of drugs or medications during storehouse because they are supplied in dry greasepaint form, which is particularly important for pharmaceuticals that are sensitive to water.
5. Prostrating needle phobia. With needle-free injections, tone- administration is possible.
7. Enhances the immunological response to vaccinations. Vaccines for Lockjaw, Typhoid fever, whooping cough, Diphtheria and Hepatitis A is suitable be administered by NFIT[3].

Needle-free Injection Technology Disadvantages:

1. Heightened risk of overdose: IV injection poses an increased risk of overconsumption. This is because the medication is swiftly introduced into the bloodstream, making it challenging to accurately determine the required dose (unlike methods such as smoking or snorting, where the dosage can be adjusted gradually until the desired effect is attained). Furthermore, due to the rapid onset of effects, overdoses can occur rapidly, necessitating immediate intervention.
2. Fear of needles: Many individuals experience a strong aversion to needles, which can sometimes induce feelings of nausea and fainting.
3. Formation of scar tissue in auxiliary routes: This results from the utilization of dull or inadequately designed paraphernalia. The formation of scar tissue can result in the darkening of these routes, and the accumulation of toxins creates grooves along their length, commonly referred to as track marks.
4. Percutaneous injury: This term refers to injuries sustained by individuals handling needles. These injuries may occur if a needle slips and injures a healthcare worker during handling. Such incidents can lead to the transmission of infections from the source person to the caregiver[4,5].

Background:

The primary means of administering drugs into the body have been Hypodermic needles and Syringes for over a century and a half. The breakthrough came in 1844 with the development of hollow needles, which enabled the first injections to be performed. However, this method was limited to drugs with specific physiochemical properties. Early syringes were simple one-piece metal devices with rubber plungers for injecting drugs. These syringes were often reused and posed challenges in terms of sterilization. The development of contemporary syringe systems incorporated medical-quality stainless steel hypodermic needles and plastic bodies, resulting in the creation of two-part disposable syringes. Despite this progress, there remained a need for more advanced drug delivery methods, especially ones capable of bypassing the skin's barrier function, known as the stratum corneum.

Throughout the history of drug development, the quest for newer and more effective delivery methods has been ongoing. The utilization of syringes as the primary vehicle for administering medications has been widespread and generally embraced, notwithstanding being linked to certain limitations.

Anatomy of the human skin:

Epidermis: The epidermis, situated on the skin's surface, is composed of Langerhans cells, melanocytes, several stratified cell layers, Merkel cells, and featuring keratinocytes. Its primary role is to act as a protective shield, both physically and chemically, safeguarding the body from external factors.

Four distinct layers of epidermis are as follows:

Stratum Basale: This is the deepest layer of the epidermis, where cell division and keratinocyte production take place.

Stratum Spinosum: The layer above the stratum basale, where cells begin to flatten and produce keratin, a protein that strengthens the skin.

Stratum Granulosum: In this layer, cells continue to flatten, and the production of keratin intensifies.

Stratum Corneum: The topmost epidermal layer, comprised of lifeless, flattened, and completely keratinized cells. It forms a protective barrier against the environment.

Dermis: The dermis is a layer of connective tissue that provides structural support and is positioned between the epidermis and the subcutaneous tissue. It houses various components, such as nerve cells, hair follicles, sweat glands, fibres, as well as lymph vessels and blood.

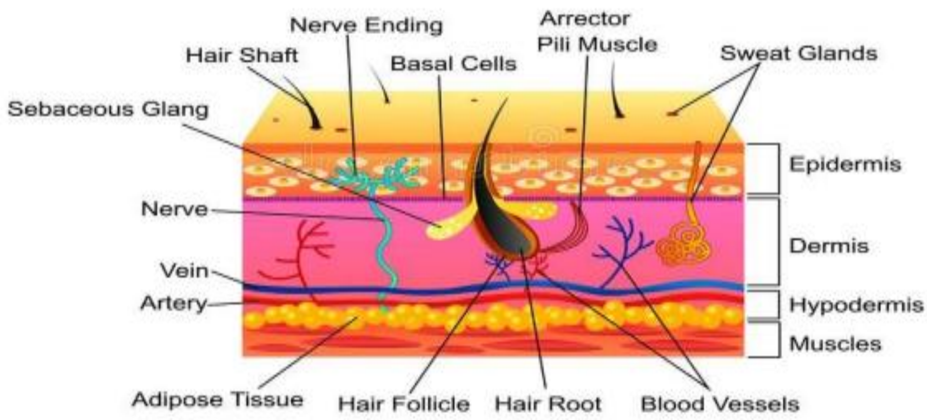
The dermis is divided into two distinct layers:

Papillary Layer: This is the thinner layer closer to the epidermis and is rich in blood vessels, providing nutrients to the epidermis. It also contains sensory receptors for touch and pain.

Reticular Layer: The thicker layer of the dermis, responsible for providing strength and support to the skin. It houses structures like hair follicles, sweat glands, and deeper blood vessels.

The main function of the dermis is to shield the body from physical pressures and demands and to provide the ability to perceive tactile sensations and temperature perception through mechanoreceptors located within.

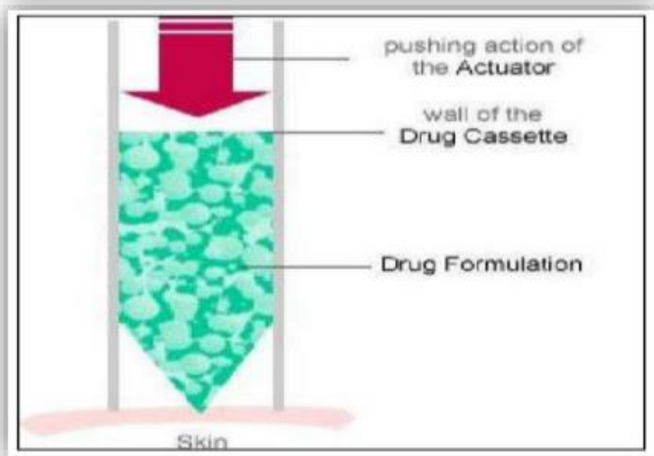
Hypodermis: The hypodermis is a stratum of loose connective tissue and adipose (fat) located beneath the dermis. Its primary function is to establish a connection between the skin and the underlying skeletal structure and muscles while supplying blood vessels and nerve endings to this region. Additionally, it serves as an energy store and contributes to body insulation[6,7].



Principle:

NFIT i.e., Needle-free injection technology employs powerful sources of energies to propel an accurately measured quantity of a particular drug composition. These drugs are loaded into distinct, specialized "cassettes" that can be integrated with the system. These energy forces can be derived from various methods, such as Intense fluid pressure, electromagnetic influences, shockwaves, or any energy form that can set the drug in motion.

Within this technology, a gas under pressure, usually air, nitrogen or carbon dioxide, generates the requisite force to expel the vaccine rapidly through a small orifice. Upon skin application, an extremely fine liquid jet swiftly pierces the skin, delivering the vaccine promptly to the subcutaneous tissue, intramuscular tissue and skin in a fraction of a second[8].



Needle-Free Injection Technology Classification:

1.Based on Operation Method

Spring-based Systems

Laser-Powered Systems

Energy-Propelled Systems

Lorentz Force Mechanisms

Gas-Propelled/Air-Forced Systems

Shock Wave Systems

2.Based on Type of Payload

Liquid Medications

Powder Formulations

Projectiles

3.Based on Drug Delivery Mechanism

Nano-Patches

Delivery Assisted by Sandpaper

Iontophoresis Facilitated

Micro-Needle Systems

4.Based on Site of Administration

Intradermal Injectors

Intramuscular Injectors

Subcutaneous injectors.

Types of NFIT Injectors:

There exist two primary categories of Needle-Free Injection Technology (NFIT) injectors.

1. Spring-Loaded Jet Injector: This type of injector functions by employing a spring mechanism that is initially tensioned backward. Upon activation of the trigger, the spring is released, producing a jet stream of the drug for dispensing. Following each use, the triggered spring must be manually reset to prepare for the next application.

2. Gas-Powered Jet Injector: This injector is equipped with an air or gas cartridge connected to the injector via a tubing system. When the trigger is activated, it releases initiates the expulsion of the piston, resulting in a jet stream of the drug. Both injector types are applicable for subcutaneous, intramuscular, or intradermal administration. The latter type will be addressed in subsequent sections. In essence, NFIT employs powerful energy sources to drive premeasured doses of specific drugs, stored in unique cassettes. These energy sources can be derived from shock waves, electromagnetic forces, high-pressure fluids and other energy forms capable of moving the medication.

NFIT technologies can be classified on the basis of their operational principles, the type of payload they handle, the mechanisms they use for drug delivery, and the specific sites on or within the body where the drugs are administered[2].

Modes of Operation in Needle-Free Injection Technology (NFIT)

By Working Mechanism

Spring System: NFIT systems use springs to store and release energy, which is a simple and effective approach. However, careful design and storage conditions are necessary to maintain spring performance, as their force diminishes with use over time.

Laser-Powered: A cutting-edge NFIT system developed by Professor Jack Yoh's team at South Korea's Seoul National University employs lasers to create tiny jets of medication that penetrate the skin precisely. The laser technology ensures drug delivery without causing tissue damage.

Energy-Propelled Systems: While conventional spring-powered jet injectors may lack control over drug pressure, energy-based systems utilize different forms of energy for drug delivery, offering more versatility.

Lorentz Force: Scientists at MIT have created a Needle-Free Injection Technology (NFIT) device that leverages the Lorentz force to expel drugs with significant pressure and velocity. The central element of the device is the Lorentz force actuator, which employs a combination of a magnet and coil to impel the drug.

Gas-Propelled/Air-Forced: Gas serves as an alternative energy source for Needle-Free Injection Technology (NFIT) systems, delivering a greater energy density compared to springs. Gas-powered apparatuses can be disposable or necessitate periodic replacement of gas cartridges. In addressing gas loss concerns, certain systems make use of carbon dioxide that has been liquefied under specific conditions.

Shock Waves: Shock waves, produced through the abrupt release of energy, are harnessed to drive medication into the skin. Scientists at the Indian Institute of Science have designed a non-invasive drug delivery mechanism that utilizes supersonic-level shock waves.

By Type of Payload

Liquid: Liquid-based NFIT systems rely on a strong liquid jet is utilized to infiltrate the skin and underlying adipose layer safely, without inducing any harm.

Powder: Powder-based NFIT systems involve formulating drug particles with sufficient density and velocity to penetrate the skin. Helium gas is often used to accelerate the drug particles.

Projectile/Depot: In this evolved version of Needle-Free Injection Technology (NFIT), the drug is molded in to an elongated, slim reservoir possessing the mechanical resilience to convey a propelling force to a pointed extremity. The reservoir can be inert or constructed from the drug substance itself.

By Drug Delivery Mechanism

Nano-Patches: Nano-patches employ applicators to deliver drugs through the skin, targeting immunocytes beneath the skin. This approach has proven effective for vaccines and is virtually painless.

Sandpaper-Assisted Delivery: Micro-dermabrasion, achieved by gently rubbing a sandpaper-like agent on the skin, removes the superficial skin layer, enhancing pharmaceutical distribution. This approach has been employed for various pharmaceuticals and vaccines.

Iontophoresis Enabled: Iontophoresis employs a small electric current to compel drug molecules to traverse the skin.

It involves two electrodes, one as a drug reservoir, and the other to finalize the electrical loop.

Micro-Needle: Miniature needle patches consist of thousands of tiny spikes that pierce transporting the drug through the outermost skin layer without reaching blood vessels or causing discomfort. These patches are suitable for vaccines and highly potent drugs.

By Delivery sites

Intradermal Site Injector: These systems provide or dispense drugs to the intradermal layer, a shallow depth within the skin. They are particularly useful for DNA-based vaccines.

Intramuscular Site Injector: Designed for administering drug into the muscle, this mechanism delivers medication deeper into the body and is highly effective for vaccinations.

Subcutaneous Site Injector: Utilized for particular proteins with therapeutic intent like hormones that stimulates human growth, these devices deliver medication to the fatty layer directly beneath the skin's outermost surface (i.e., adipose layer).

Prerequisites for needle-free injection technology i.e., NFIT'S:

Drug Requirements

Products lifespan: Non-prefilled devices must have an extended products lifespan achievable through a stable power source, ensuring they remain functional even after a storage period of 2 to 3 years under varying circumstances. For prefilled needle-free injection technology (NFIT) systems, several considerations are crucial throughout the planned duration of viability: a. Maintaining the sterility of the product. b. Ensuring endotoxins and foreign particles stay within specified limits. c. Monitoring the leaching of substances from device components into the drug formulation to ensure it remains acceptable. d. Preserving the purity, composition, and concentration of the drug throughout the intended shelf life. e. Using materials for the entire device that are stable, mechanically strong, economical and non-reactive.

Viscosity: As new medicinal formulations often involve larger molecules and require higher concentrations, viscosity becomes a significant factor. Conventional needle and syringe setups demand increased pressure to inject more viscous preparations. However, needle-free devices excel in administering a diverse array of formulations with different viscosities, as they do not rely on hollow needles[9,10].

Mechanism:

A spring-contained body generates the force to expel the drug through the opening at an exceptionally high velocity.

This ultra-fine fluid stream penetrates the skin layer for rapid drug delivery into the systemic circulation.

The entire drug delivery process through injection occurs in less than one-third of a second.

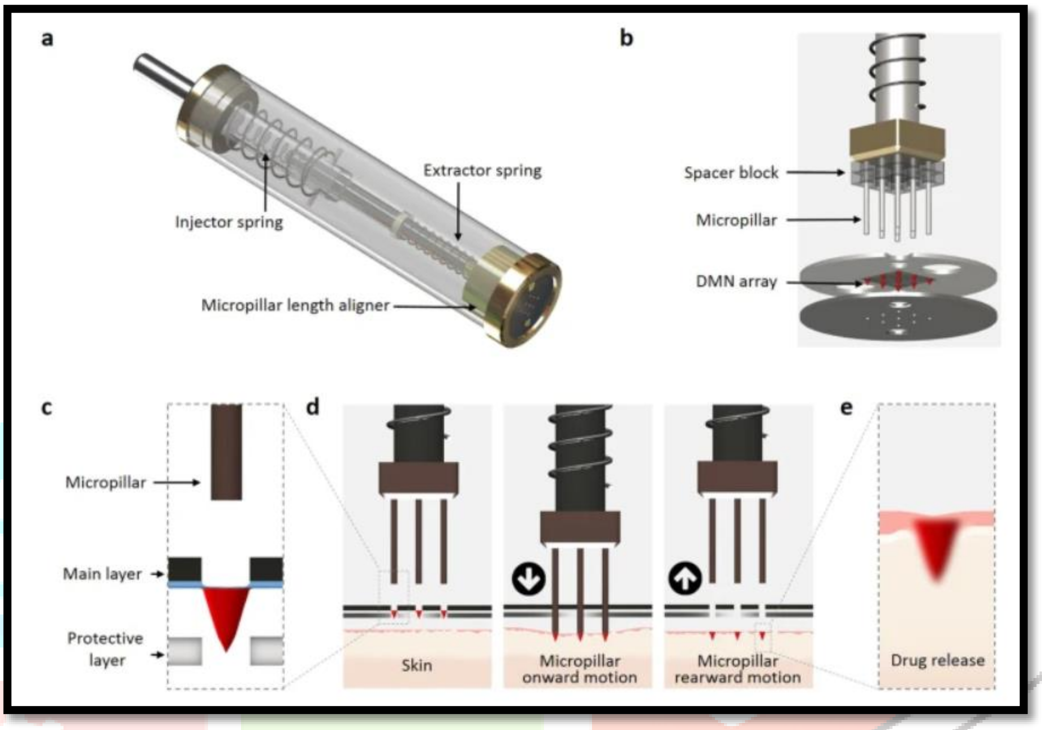
The needle-free drug delivery involves three main stages:

1. Phase of Peak Pressure: This phase utilizes the ideal pressure to permeate the skin (less than 0.025 seconds).
2. Phase of Delivery or Dispersion: Lasting up to 0.2 seconds.
3. Drop-off Phase: Occurring in less than 0.05 seconds.

The entire duration for vaccine delivery is within the range of 0.5 secondstotal time required to deliver the vaccine is up to 0.5 seconds.

Administration of medication via needle-free injection involves the following steps:

1. Load the medication into the injector body.
2. Choose the injection site. Disinfect the skin at the injection site to prevent contamination that might cause discomfort.
3. Remove the injector cap, gently stretch the skin at the injection site, and mark the site using a 'J tip.'
4. Administer the medication by pressing the actuator. Wait for 2-3 seconds after injecting before removing the 'J tip.'



Manufacturing of Needle-Free Injection Technology:

Raw Material: Materials used in needle-free devices must be pharmacologically inert since they come into direct contact with the skin. Polycarbonates and thermoplastics, lightweight synthetically produced materials, are ideal for the device's outer components. Helium or CO are the gases used for gas-powered systems, is used for propulsion, and newer designs utilize butane. The materials must not react with gases or other components.

Making the Pieces: Injection molding is a adaptable procedure used in manufacturing of plastic for crafting needle-free devices. Pellets of suitable raw materials are fed into a hopper, which directs them to the machine's cylindrical body via a rotating screw. The melt is injected into a mold, where it cools and hardens under pressure. The mold is opened to eject the formed design, which is inspected for defects.

Labeling: the designed structure moves to a production line, where machines apply markings for dose levels, and compartments are inserted to create a complete device. Attachments, if needed, remain constant at this phase.

Packaging: The fully assembled device is wrapped in sterile films, placed in cardboard or plastic boxes, and accompanied by necessary manuals and inserts. The boxes are arranged in stacks on pallets in preparation for shipment.

Quality Control (QC): The manufacturing procedure is closely monitored for Visual imperfections, structural deformities, equipment accuracy, dimensions, thickness, labeling, and calibration. The devices are subject to strict control by the FDA, which conducts inspections at regular intervals to ensure safety and quality [4,5].

II. CONCLUSION

The progress of skin-penetrating drug delivery systems has depended on fundamental engineering principles. Needle-free technology offers a solution to the drawbacks associated with traditional needle and syringe systems, such as pain, Fear of needles and unintentional needle pricks. These instruments can effectively administer a diverse array of medicinal formulations into the body, maintaining equivalent biological effectiveness as traditional syringe systems but without the unnecessary pain and complications. Needle-free devices are user-friendly, require no expert handling, easy storage and disposal. They are suitable for administering drugs to sensitive areas like the cornea and are effective for various types of injections. Considerable resources have been allocated to the advancement of this technology, resulting in the availability of numerous devices in the market following FDA approval[11].

III. APPLICATIONS

Needle-free injection technology has various applications:

1. It is employed in mass immunization programs for diseases like measles and smallpox.
2. Intraject technology, developed by Weston Medical, is used for the wide range of drug delivery, including peptides, proteins, small molecules, vaccines and monoclonal antibodies.
3. Powderject technology, from PowderJect Pharmaceuticals, delivers substances like inulin to hairless guinea pigs and is Utilized for introducing DNA immunization into the skin as a defense against influenza virus in mice. It's especially effective for transporting large macromolecules through the skin.
4. Jet injectors are utilized to administer proteins such as β-interferon and traditional therapeutic substances such as lidocaine (lignocaine) for localized numbing.
5. The DSJI (i.e., Disposable Syringe Jet Injector) supports clinical research focused on delivering vaccinnations using jet injectors[12].

IV. REFERENCES

1.Barolet, D. and Benohanian, A., 2018. Current trends in needle-free jet injection: an update. Clinical, cosmetic and investigational dermatology, pp.231-238.

2. Ravi, A.D., Sadhna, D., Nagpaal, D. and Chawla, L., 2015. Needle free injection technology: A complete insight. *International journal of pharmaceutical investigation*, *5*(4), p.192.

3.Scanlon Daniels,” 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

4. Stachowiak JC, Li TH, Arora A, Mitragotri S, Fletcher DA,: “Dynamic control of needle-free jet injection”, University of California, Berkeley, Department of Mechanical Engineering, Berkeley, CA 94720, USA.

5. Daneil CS., “Needleless injections-Good, Bad or Ugly?” Proc. ISU Swine Dis Conf. 2005:28-30

3. Kohle S, Sontake S. A review on needle free drug delivery system. Int J Pharm Pharm Sci. 2013;5:15–20.

4. Ren T, Wang X, Yang PH. Vaccine and Needle free vaccination delivery system. J Microb Biochem Technol. 2014;6:359–60.

5. Potter C. Caretek Medical Device. Management Forum Conference on Needle-Free Injection Systems and Auto-Injectors.

6. 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.

7.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. 4/6/22, 7:24 PM Needle free injection technology: A complete insight https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4675000/ 14/14

8. Prausnitz MR, Langer R. Transdermal drug delivery. Nat Biotechnol. 2008 26:1261–8.

9. Daddona P. Transdermal technology: Macroflux transdermal technology development for the delivery of therapeutic peptides & proteins. Drug Deliv Technol. 2002;2:54–7.
10. Pray WS, Pray JJ. Blood glucose meters: A dynamic market. US Pharm. 2002;27:18–23.
11. Cygnus, Inc. Sankyo Pharma and Cygnus Announce FDA Approval for Pediatric Use of GlucoWatch G2 Biographer.
12. Taddio A, Ipp M, Thivakaran S, et al. Survey of the prevalence of immunization non-compliance due to needle fears in children and adults. Vaccine. 2012;30(32):4807–4812.