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NEEDLE FREE INJECTION SYSTEM

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- **ABSTRACT**

This project introduces a groundbreaking needle-free injection system, designed to transform the way vaccines and medications are administered in various settings, including the swine industry. The system eliminates the need for traditional needles, offering a rapid and effective route of administration. By leveraging electrophoresis technology, the device enables transdermal drug delivery, ensuring improved patient comfort and reduced risk of needlestick injuries. The reusable and disposable designs cater to diverse user needs, from at-home use to institutional and multi-patient settings. A crucial aspect of this innovation is an enhanced educational program, essential for ensuring the safe and successful adoption of needle-free injection systems in swine operations. By addressing the risks associated with needleless injection, this project aims to promote a paradigm shift in drug delivery, enhancing the overall efficiency, safety, and efficacy of healthcare practices.

KEYWORDS: Needle-free, Skin, safety, pain-free, Liquid, Intramuscular, Intradermal.

INTRODUCTION

The phrase "needle-free" refers to various drug delivery technologies that do not involve needles, such as those that utilize electrophoresis to administer drugs through the skin, as well as technologies that employ very small needles. Needle-free devices can be found in numerous forms, including potent sprays, edibles, inhalers, and skin patches. These devices are available in both reusable and disposable formats, suitable for use at home or in healthcare settings, and come in versions for multiple patients and institutional use.

Techniques for needle-free injections can be utilized to deliver vaccines and medications in the swine industry. This method offers a fast and efficient means of administration. However, there are risks that need to be addressed to ensure the safety of workers operating needleless injection systems. As a result, a comprehensive training program is essential for the effective implementation of needle-free injections in any swine facility. Needle-free injection systems represent innovative methods for administering various medications without the need for traditional needle punctures.

- **HISTORY**

The initial syringes were created by French surgeon Charles Gabriel Pravaz in 1853. The design of syringes has seen minimal changes, as the technology has been fairly consistent for the past 150 years. Marshall Lockhart first referred to needleless systems in 1936 when he patented an injection method for aircraft. Subsequently, in the early 1940s, Higson and others pioneered high-pressure "guns" that utilized a liquid stream to penetrate the skin and deliver medication to the underlying tissue.

Since the therapeutic properties of medicines have been established, individuals have sought improved methods of delivery. In the early 1800s, scientists made various discoveries that ultimately resulted in the creation of the hypodermic needle by Alexander Wood in 1853. This instrument was employed to administer morphine to patients with sleep disorders. Over the subsequent years, the hypodermic needle underwent considerable modifications that enhanced its effectiveness, safety, and reliability. Nevertheless, needles still possess notable drawbacks that have led researchers to explore alternatives that do not require a needle.

- **OBJECTIVES**

1. Examine needle-free injection systems and outline the various types available.
2. They are less painful and may offer greater safety.
3. The primary benefits of using a needle-free system and the simplicity of a liquid jet injector do not compensate for the higher costs associated with these products compared to other delivery options.
4. The key benefits of needle-free systems include the removal of broken needles, improved consistency in administering vaccines and medications, and decreased risks to occupational safety.

- **Advantages**

Here are the benefits of needle-free injection systems:

1. They alleviate patients' fear of needles.
2. They mitigate the possibility of needle breakage.
3. They lower expenses.
4. They enhance patient adherence to treatment while decreasing the volume of the vaccine.
5. They lessen pain and anxiety.
6. They focus on stimulating the immune response.
7. They minimize the number of injection site wounds.
8. They enable continuous vaccine administration.
9. They prevent cross-contamination.
10. They exhibit an excellent dose-response relationship with higher drug dosages.
11. Bioequivalence has been established, facilitating the creation of generic drug proteins.
12. They offer rapid administration and reproducibility that is comparable to traditional needles and syringes.
13. They enhance bioavailability in comparison to other non-invasive or less invasive drug delivery methods.
14. They improve the immune response to both DNA and conventional vaccines.
15. They allow for modifications in the pharmacokinetics of certain medications.

Disadvantages

1. There is a risk of cross-contamination from needles.
2. Inadequate or excessive dosing may result from poor injection techniques.
3. Fear of needles persists.
4. Discomfort at the injection site may occur.
5. Low patient compliance can lead to deteriorating long-term health conditions.

   Increased expenses may arise from patients needing to visit hospitals for injections.

- **Benefits**

Improved Clinical Results

1. A substitute for needle-based methods or electroporation.
2. Enhanced effectiveness in comparison to N/S.

3. Similar in performance to electroporation.

Validated Commercial Device

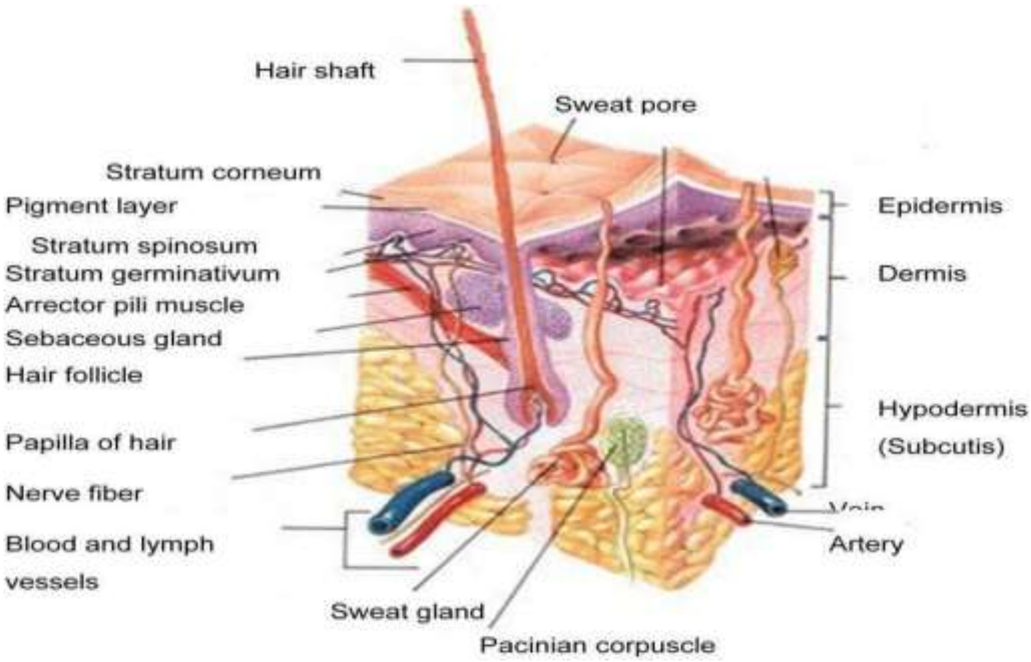
1. The administration of 0.5 ml via intramuscular or subcutaneous routes.
2. Presents a potential for dose optimization.

Improved Patient and Caregiver Experience

1. Enhanced adherence to vaccination protocols.
2. Assurance of safety and comfort.

- **Structure of human skin**

Understanding the anatomical composition of the skin is crucial for the effective administration of pharmaceuticals via needle-free injection systems, as these medications are administered directly onto the skin's surface.



Structure of human skin

Human skin generally consists of two layers.

1. Pidermis
2. Dermis

Epidermis

The epidermis represents the outermost layer of the skin, serving as a protective and impermeable barrier on the body's surface. It is composed of squamous epithelium, which is supported by an underlying lamina propria. Notably, the epidermis lacks blood vessels; instead, the cells in its deeper strata receive nourishment through the diffusion of blood capillaries that extend into the upper layers of the dermis. The primary cell types found within the epidermis include Merkel cells, keratinocytes, melanocytes, and Langerhans cells. This layer can be categorized into several distinct strata, beginning with the outermost layer: the stratum corneum, followed by the stratum lucidum (present only on the palms and soles), the stratum granulosum, the stratum spinosum, and the stratum basale.

Stratum germinativum

The structure comprises columnar keratinocytes that are attached to the underlying basement membrane, oriented with their long axis perpendicular to the dermal layer.

Strum spinosum

The thickness of the structure ranges from 5 to 10 cells. The intercellular spaces among the spinous cells are linked by a multitude of desmosomes, which serve as adhesion points. These desmosomes facilitate the cohesion of epidermal cells and contribute to their resilience against physical stress.

Strum granulosum

The structure comprises living cells that play a crucial role in the synthesis and subsequent modification of proteins associated with keratinization. Its thickness ranges from one to three layers of cells.

Stratum corneum

Coenocytes are characterized by a high protein content and a low lipid concentration, exhibiting hydrophilic properties, and are enveloped by a continuous extracellular lipid matrix.

Malpighian strata Layer

The protoplasm of which has not yet undergone transformation into keratinous substance.

Dermo-epidermal layer

The structure serves as a foundational element for the epidermis, facilitating the establishment of cell polarity and guiding the direction of growth. It orchestrates the organization of the cytoskeleton within basal cells, delivers essential developmental signals, and operates as a semipermeable barrier that separates various layers.

Dermis

The dermis is situated beneath the epidermis and is primarily composed of connective tissue, serving to safeguard the body against stress and strain. This layer is intimately linked to the epidermis through a basement membrane. Additionally, the dermis houses numerous mechanoreceptors, which are nerve endings responsible for the sensations of touch and temperature. It also contains various structures, including hair follicles, sweat glands, sebaceous glands, apocrine glands, lymphatic vessels, and blood vessels. The blood vessels within the dermis play a crucial role in supplying nutrients and eliminating waste products from both the dermal cells and the basal layer of the epidermis.

Hypodermis

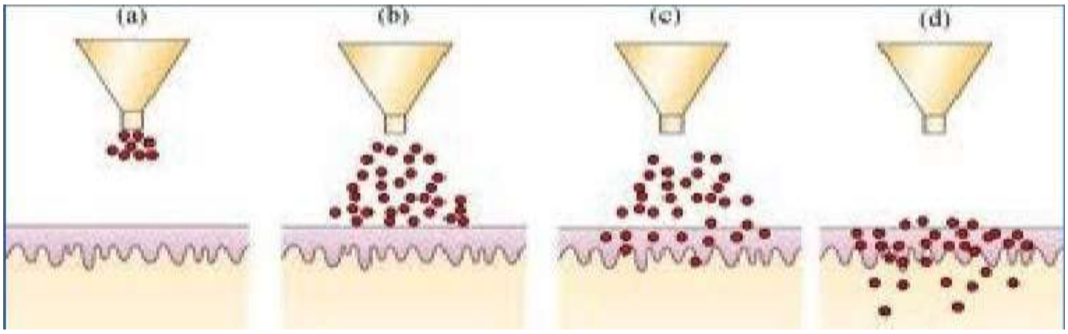
The hypodermis, while closely associated with the skin, is classified as a distinct layer of subcutaneous tissue that comprises adipose and connective tissue. Its primary functions include anchoring the skin to the underlying skeletal and muscular structures, in addition to providing a network of blood vessels and nerves. This layer is characterized by its loose connective tissue and the presence of elastin fibers.

- Type of needle free injection

1. Powder injections
2. Liquid injections
3. Depot or Projectile Injection

Powder injections

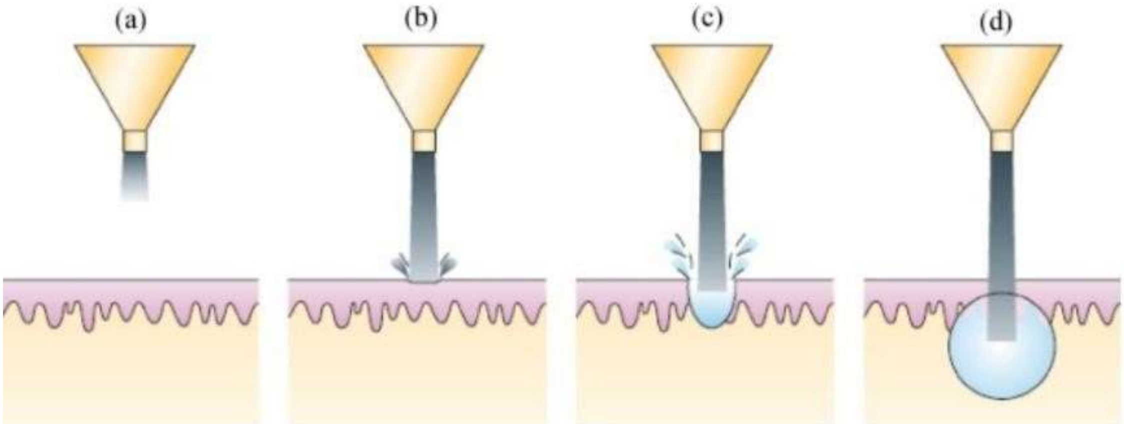
These devices are designed with a chamber containing solid drug formulations and a nozzle that facilitates the delivery of drug particles into the skin through the use of compressed gas as a propulsion mechanism. The medication is administered in a powdered form rather than as a liquid, resulting in a painless injection experience. Each side of the chamber is equipped with a diaphragm that is only a few microns thick, effectively sealing the drug chamber. To achieve sustained release or enhance the therapeutic efficacy of the drug, bioerodible carriers, slowly dissolving excipients, less soluble salts, or disintegration agents can be employed. Additionally, protein-based medications are particularly potent and well-suited for these needle- free powder injection systems.



Mechanisms of powder injections

Liquid injections

The fundamental concept underlying this injection method involves creating a sufficiently elevated pressure from a liquid that is in close proximity to the skin, enabling the liquid to penetrate the skin by creating an opening. These systems typically incorporate mechanisms such as gas or springs, pistons, compartments containing the drug, and nozzles with orifices measuring approximately 150 to 300 μm in diameter.



Mechanisms of liquid injection

Advantages of liquid injections

1. A minimal quantity of substance, administered transdermally as a powder rather than a liquid, results in a painless injection experience.
2. The therapeutic compound exhibits enhanced stability and eliminates the requirement for refrigeration.
3. The sustained release of the drug or its efficacy can be accomplished through the utilization ofbioerodible carriers, gradually dissolving excipients, specific less soluble salts, or dissolution enhancers.

4. Protein-based pharmaceuticals are highly effective and well-suited for needle-free injection systems utilizing powdered formulations.

Depot or projectile injection

These systems are engineered to administer pharmaceuticals directly into muscle tissue. They establish a reservoir of medication within the muscles, which is released gradually over a specified duration. This technology is commonly referred to as needleless projectile injection technology and represents a significant recent innovation. In this method, the drug is prepared as a slender, elongated deposit that is robust enough to transmit the necessary force through a pointed tip, which is constructed from an inert, soluble material such as sugar. The deposit is forcefully embedded into the skin, allowing it to penetrate both the epidermis and subcutaneous fat. Typically, the deposit measures approximately 1 mm in diameter, which is adequate for the delivery of most proteins and antibodies. A pressure range of 3 to 8 megapascals (MPa) is sufficient to breach the skin using a pointed mechanism. This approach is particularly advantageous for medications that are effective in the milligram dosage range and for those whose liquid formulations may be unstable.

- **Types On the basis of site of delivery**

1. Intradermal injector

These systems have been utilized to administer relatively novel DNA-based vaccines to the intradermal layer. The delivery mechanism targets a superficial depth, specifically within the skin's layers.

2. Intramuscular injector

One of the most advanced needle-free injection technology systems utilized for intramuscular drug administration is noted for its capability to deliver medications at significant depths. This method of drug delivery is recognized as the most effective among all available options. Furthermore, needle-free injection technology devices have demonstrated considerable success in the realm of vaccination.

3. *Subcutaneous injector*

Certain therapeutic proteins, such as human growth hormones, have been administered through this system. The medication is delivered to the adipose tissue located just beneath the skin.

Table 1: Market product of liquid-based needle free injection.

Product Name	Company	Type of system
Intraject	Weston medical	Liquid-based needle free injection
Medijector vision	Antares Pharma Inc	Liquid-based needle free injection
Penjet	Penjet corporation	Liquid-based needle free injection
Med-E-Jet	Evans enterprise	Liquid-based needle free injection
Advantaget	Advantage health services	Liquid-based needle free injection
Gentlejet	Health for personal care	Liquid-based needle free injection
J-tip	National medical products, inc	Liquid-based needle free injection
Injex	Equidyne Systems, Inc	Liquid-based needle free injection
Powderject system	Powder ject pharmaceuticals	Powder-based needle free injection
DepixolDepo injection	Lundbeck Limited	Depot based needle free injection

- **MECHANISM OF WORKING**

Needle-free injection technology operates by propelling liquid medication at high velocities through a minuscule orifice that is pressed against the skin. The diameter of this orifice is less than that of a human hair, resulting in an ultrafine stream of high-pressure fluid that penetrates the skin without the use of a needle.

The design of the injection device significantly affects the precision of subcutaneous delivery and the stresses experienced by the medication being administered. It is essential for the design to generate sufficient pressure to breach the skin, while subsequently reducing the pressure to ensure that the medication is deposited at a depth that does not reach the muscle tissue. High-pressure delivery poses a risk of damaging delicate molecules, such as monoclonal antibodies. Consequently, the effective delivery of these molecules necessitates a device with meticulously controlled power parameters. Numerous companies are engaged in the advancement of this technology, including Antares Pharma Inc., Aradigm Corporation, Bioject Medical Technologies Inc., and Biovalve Technologies Inc.

- **THE FUTURE**

Numerous needle-free alternative technologies are currently in the developmental phase. Companies are actively engaged in creating devices that prioritize safety and user-friendliness. Additionally, efforts are underway to develop alternatives capable of administering a broader range of medications. Enhancements are being made to inhalers, nasal sprays, forced air injectors, and transdermal patches. Looking ahead, there is potential for certain foods to be genetically modified to serve as vehicles for vaccines and other pharmaceuticals, with bananas and tomatoes being notable examples. Research is underway to explore the feasibility of using bananas as carriers for a vaccine aimed at combating the

Norwalk virus, while tomatoes are being engineered to provide protection against Hepatitis B. Beyond the innovation of new delivery systems, scientists are also exploring strategies to create longer-lasting medications, thereby minimizing the frequency of needle-based injections.

- **CONCLUSION**

The detrimental impact of needle phobia and accidental needle-stick injuries on patient compliance and overall healthcare cannot be overstated. Fortunately, needle-free technology has emerged as a viable solution, offering a painless and efficient means of delivering a wide range of medicinal formulations into the body with equivalent bioequivalence to traditional syringe systems. The simplicity, safety, and versatility of these devices make them an attractive alternative for administering medications to sensitive areas, such as the eye, and for various injection routes, including intramuscular, subcutaneous, and intradermal. By adopting needle-free technology, healthcare providers can alleviate patient anxiety, reduce the risk of accidental needle-stick injuries, and improve overall patient outcomes. As the healthcare landscape continues to evolve, the integration of needle-free technology is poised to play a vital role in shaping the future of medication administration.

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