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MEDICATED TATTOOS: A RECENT DRUG DELIVERY APPROACH IN MEDICAL SCIENCE

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ABSTRACT: Transdermal drug delivery systems are potential sources of administering drugs through and have certain advantages as delivering a therapeutically effective amount of drug across a patient's skin. Medicated Tattoos is one of the upcoming approaches in transdermal drug delivery. Researches reveal that humans from the generations have used tattoos for various reasons like symbol of rank, religious/spiritual devotion, and decoration for bravery, sexual temptation as well as to express the love. In the past years, there are various reported cases of syphilis, tetanus, tuberculosis, and herpes that have been associated with tattooing. Many of these infections resulted from mixing saliva with ink or tattooists holding needles in their mouths. Medicated tattoos are becoming a very popular drug delivery system, as tattoos are trendy among adolescents. There are so many recent advancements in the field of medicated tattoos. Recently, the tattooing has been widely used as a drug delivery system in the field of medicine (corneal tattooing, gastrointestinal tattooing during endoscopy, permanent make-up tattooing, scar camouflage, or radiotherapy field was marking.

INTRODUCTION: Tattooing has gained remarkable recognition for the past twenty years. It is derived from a Tahitian word 'tatu' which means to mark something for symbolic representation or identification. Researches reveal that humans from the generations have used tattoos for various reasons like symbol of rank, religious/spiritual devotion, and decoration for bravery, sexual temptation as well as to express the love. In the past years, there are various reported cases of syphilis, tetanus, tuberculosis, and herpes have been associated with tattooing.

In the recent arena, tattooing has also found its way in the field of medicine (corneal tattooing, gastrointestinal tattooing during endoscopy, permanent make-up tattooing, scar camouflage or radiotherapy field was marking ¹. Recently, the tattooing has been widely used as a drug delivery system in the field of medicine (corneal tattooing, gastrointestinal tattooing during endoscopy, permanent make-up tattooing, scar camouflage or radiotherapy field marking. Many of these infections resulted from mixing saliva with ink or tattooists holding needles in their mouths ².

Modern Tattooists use the Following Steps:

- Firstly, the needles are soldered onto a distinct moveable shaft called the "needle bar" which is inserted into a stainless steel tube that serves as the "grip".
- These items are then sterilized.

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- Then the needle bar is dipped in different pigments to outline a design and fill in the color varying from 1-14.
- Needle bar & tube assembly are mounted onto a direct current (DC) powered machine that vibrates the needle bar causing the needle to protrude out of the base of the tube.
- Finally, the needles penetrate the outermost layer of the skin (the epidermis) and reach the next layer (the dermis).

As technological advancement, this conventional tattooing is transformed in the form of a transdermal drug delivery system.

Transdermal drug delivery systems are a potential source of administering drugs through and have certain advantages as delivering a therapeutically effective amount of drug across a patient's skin. Transdermal has the advantage over needle injections and oral routes. It has great patient compliance and avoids demerit of the oral route by eliminating fast pass metabolism³.

In the case of TDDS, the drug must be able to penetrate the skin so that the drug can easily reach the target site. Certain factors should be considered during using Transdermal drug delivery as high potency, better permeability through the skin, and non-irritation for better compliance.

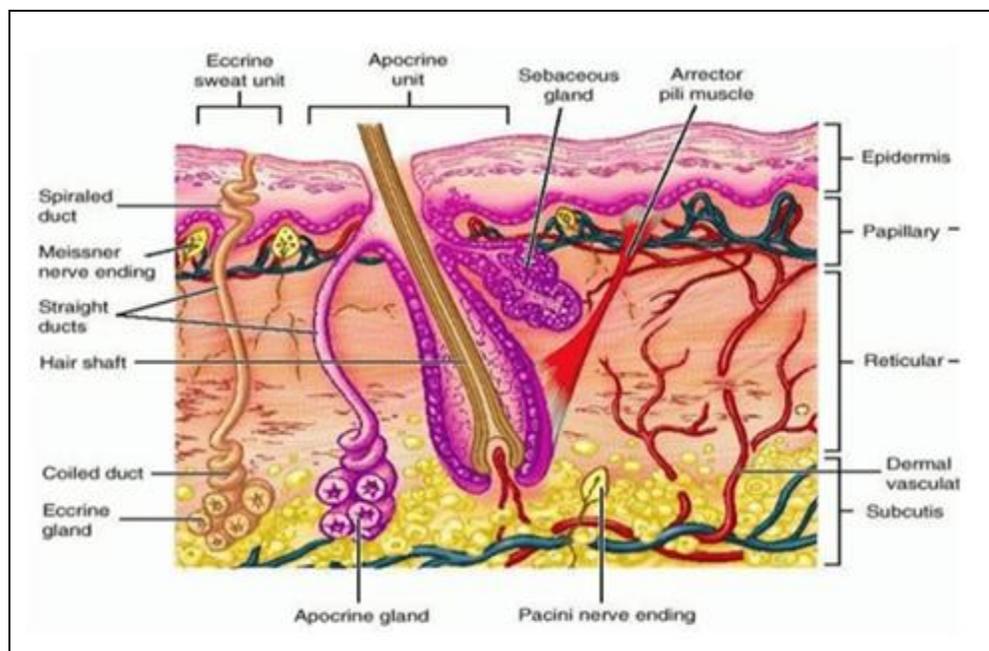


FIG. 1: BASIC STRUCTURE OF SKIN⁴

Medicated Tattoos is one of the upcoming approaches in transdermal drug delivery. Medicated Tattoos Med-Tats is a modification of temporary tattoo as the normal tattoo is used for fun similarly Medicated tattoo contains the active ingredient of medicament. It is easily attractable for small children who have a fear of injection or other few drug delivery, which are inconvenient for them. Several pharmaceuticals pay greater attention in case of choosing ingredients to increase penetration through skin, mostly substances, like alcohol, within the patch to improve their penetration via skin to improve absorption. These Med-Tats prototypes contain acetaminophen and vitamin C as the drug candidate.



FIG. 2: COMPLICATION OF TATTOOING⁵

The Formulation of Medicated Tattoos: The formulation & composition of tattoos:

- A drug layer
- A color design layer
- An adhesive layer (binds to the skin)

A patch of tattoo is loaded with drugs and usually applied on the skin to transport a specific dose of medication across the skin and into the blood circulation⁶. There are two major functions of the adhesive: It is the glue in nature that keeps the patch adhered to the skin, and it acts as the suspension that holds the drug. The problems associated with this is the concentration of the drug within the adhesive directly affects the "stickiness" of the adhesive so if the large quantities of the drug are to be administered, either the size of the patch has to be increased or the patch needs to be reapplied again and again.

The drug candidate as well as other pharmaceuticals usually combined with substances, like alcohol, within the patch to improve their penetration *via* skin to improve absorption. They are also applied to clean dry skin in the same manner⁷.

Tattoos are temporary to permanent marking in the skin, usually made by the ink & needle. Once the ink is deposited into the dermis, the second layer of the skin scrubs over; then the skin heals to expose a design under the new layer of skin. When it's completely healed, its beautiful on the body called a tattoo. This is the concept of natural tattooing. A tattoo will fade if the immune system ever succeeds in breaking up the pigment particles.

The concept of "Medical tattooing is highly similar to the existing regular tattooing, except here non-allergic ink is introduced into the dermal layers of the skin (deeper layers of the skin)," Medical tattooing is also recommended for patients who have had breast reconstruction surgery and has been proved as better and effective drug delivery systems. At the same time, women also do medical tattoos to cover scars left on the breast after surgery. Tattooing based drug delivery systems are also used to treat Cutaneous Leishmaniasis⁸. Tattooing is widely used in medical research to deliver the concept of DNA vaccination strategy. Medicated Tattoo (Med-Tat) is a modification of temporary tattoo which contains an active drug substance for transdermal delivery.

Tattoo inks are solutions comprised of a carrier and a colorant. The carrier is the fluid that is used to transport the colorant to the application location. It may contain glycerin, water, isopropyl alcohol. Apart from that, there are so many other methods of tattooing like removable transdermal tattoos, which are further explored as the medicated tattoos in which the active drugs are incorporated along with the ink base to fulfill the desired action.

The Basic Mechanism behind Medicated Tattoo:⁹

- It is applied to clean and dry skin.
- A patch of tattoo is loaded with active medicament and applied on the skin to transport a specific dose of medication across the skin to obtain the desired therapeutic effect.
- It contains an adhesive that keeps the patch adhered to the skin and also acts as the suspension that holds the drug.
- The manufacturer provides a color chart so that it can be compared to the color of the patient's tattoo to determine when the tattoo should be removed.
- The key visual comparison relies on the dyes which are incorporated into the patch, introduces a significant amount of inter-patient variability.

Advantages of Tattoos as Drug Delivery System:

- The key advantage of medicated tattoos is the delivery of drugs to children who cannot tolerate the conventional dosage form.
- These are very attractive & easy to wear as these are gently applied by wetting with water and pressing against the skin with the nominal force of application.
- It improves the ultimate appearance of the skin.
- It is considered to nourish skin as many are specially formulated with nutrients and vitamins to enhance and expedite the healing process.
- It prevents infections as moisturizing the tattooed area stops scabs from forming and seals lacerations to keep bacteria from spreading¹⁰.

Disadvantages and Associated Risks of Tattoos as Drug Delivery System: There are potential health risks & complications related to tattooing like infection, tattoo-associated dermatoses & allergic reactions¹¹:

- There are chances of getting cancer, as it contains cancer-causing agents.
- There are chances of getting Hepatitis due to the use of needles.
- Furthermore, there is associated pain due to penetrating the needle deep into the skin.
- There are cases of skin rashes.



FIG. 3: TATTOOS RELATED TO ALLERGIC REACTIONS¹²

Indication of the Complete Drug Absorption:

There is a visual indication as to the drug absorption starts and when it is completely absorbed into the skin. For this purpose, the manufacturer provides a color chart that is compared to the colors of the medicated tattoo applied to the patient as it determines when the tattoo should be removed. Upon absorption, the tattoos gradually fade away and are painless to remove with the help of simple astringent wash containing isopropyl alcohol. The drugs used in medicated tattoos have some prototype drugs as Acetaminophen, vitamin C, etc.

Current Status of Medicated Tattoos: There is a patent US patent PCT/US2001/043422 on medicated tattoos, which is a transdermal medicament delivery device in the form of a printed temporary tattoo. This research project was emphasized on developing the transdermal tattoos includes lithographic printing and silkscreen coating, to create the necessary layers, inclusive of drug deposition on the control membrane. Medicated tattoos are becoming a very popular drug delivery system as tattoos are trendy among

adolescents. Medicated tattoos are the modification of general temporary tattoos containing the active medicaments, delivering the drug by the transdermal route as a part of the transdermal drug delivery system¹³.

Another type of such tattoos is medical alert tattoos or medical wrist tattoos/medical information tattoos. Due to a great and emerging application of tattooing for medical identification for conditions requiring special attention during emergencies, such as patients with diabetes who may be found unconscious due to hypoglycemia or with an allergy to specific medication¹⁴. Also, in the case of Amalgam tattoo, an iatrogenic lesion is caused by traumatic implantation of dental amalgam into a soft tissue, typically on the gums of the lower jaw to attain a trendy look.

Application of Tattoos for the Indication of the Disease State for Emergency Help: Tattoos can be used to indicate the disease state of a person to be helped in the disease states with critical time like in case of diabetes, epilepsy and heart strokes.

Hence, in this case, by looking at such tattoos, the medical emergency can be identified, and the patient should be immediately supported by the recommended health support.



FIG. 4: EXAMPLE OF TATTOO FOR MEDICAL EMERGENCY ALERT¹⁵

Recent Advancement in the Field of Medicated Tattoos: There are so many recent advancements in the field of medicated tattoos. One of them is electronic tattoos, which measure the emotions by tracking muscle and nerve activity, representing a recent example of medicine with devices, reflecting skin as a digital platform, at the same time reducing the need for painful needles. Some researchers at

the Center for Wearable Sensors at the University of California, San Diego, have developed a removable electronic tattoo that can sense your blood-alcohol level from the sweat on the skin of humans and then send this information *via* Bluetooth to a Smartphone or car computer.



FIG. 5: TATTOO-BASED TRANSDERMAL ALCOHOL SENSOR¹⁶

Furthermore, other recent devices have wireless sensors that can monitor a person's activity. Researchers have used the skin electrodes-based wearing tattoos to monitor the muscular and neuronal activity of a patient suffering from a neurodegenerative disease like Alzheimer's disease. Similarly, wireless skin biochemical sensors have been developed and applied in the form of wearing tattoos, the best example of electronic tattoos research. Recently, Graphene-based wearable electronic tattoos are developed to monitor the health of the human body, enabling their biometric uses, such as monitoring of the electrical activity of the brain, heart, and muscles. Similarly, gold and titanium-based electronic tattoos are also developed, offering significant relevance in the medical science for medical alerts of various chronological diseases. There are various electronic tattoos printed on skin used to transmit medical data in the healthcare industry.

Organizational Impact of Wearing Tattoos:

There are huge psychological and psychiatric aspects of tattoos in society. But it has the gender-specific as well as occupational specific acceptance in the society. According to a survey, 58% of employers would be less likely to offer a job to a tattooed applicant. It means it reflects the organizational attitude towards wearing tattoos. At the same time in a society wearing tattoos is the sign of indiscipline behavior¹⁷.

Statistics about tattoos in the workplace revealed. According to the research, almost 76% of employees feel tattoos and piercings hurt job interview chances, 73% of people say they would hire staff that had visible tattoos, 6% of tattooed people say they wouldn't hire someone with visible ink, only 4% of tattooed or pierced people say they've faced discrimination at their current job.

Government Regulations for Tattooing: The ink and other ingredients used in the tattooing may contain harmful microbes as well as may develop allergic reactions hence tattoos, and their potential health consequences should be assessed as per the set regulations¹⁸. Moreover, Drugs & Medical Devices Group is responsible for conducting on-site inspections of tattoo and body piercing studios. During these inspections, we ensure that the studios comply with state and local laws and regulations. Furthermore, it varies with location on the national and international front. There is a need for sterilization records showing routine sterilization practices. There is a licensing guideline for the tattoo parlor, and there are so many concerns for minors. The tattooist reports any infection or adverse reaction to the Department of State Health Services. The primary risks monitored under these regulations are the possibility of infection and the transmission of disease through unsanitary procedures or conditions.

CONCLUSION: Medicated tattoos as a transdermal drug delivery system have been recognized as a potential delivery system in spite of its limitation. This drug delivery system brings rate-controlled delivery with fewer side effects, increased efficacy, and constant delivery. Human skin has been proved as an extremely good barrier function, and to improve the penetration of active ingredients, it is frequently necessary to employ enhancement strategies. Furthermore, tattooing has gained tremendous popularity in medical science. There is a well-established emerging application of tattooing for medical identification for conditions requiring special attention during emergencies, such as patients with diabetes who may be found unconscious due to hypoglycemia or with an allergy to a specific medication. In the current issue, the treatment options for tattoos are well described, and further, it requires individualization as per the safety concerns of the patient. It serves as

a reliable and efficacious tool in treating amateur, professional, cosmetic, and traumatic purposes. Moreover, by incorporation of nontoxic and non-irritant biodegradable herbal pigments in the medicated tattoos can trigger the explosion in the medical science arena.

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