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Recent Development in Vaccine Delivery System: From Oral to Transdermal Route

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Abstract: *The methods by which vaccines are delivered have changed dramatically in the last ten years. This change has been primarily influenced by factors such as the need to have better patient compliance, faster global immunization strategies, and improved immune responses. Traditional injectable vaccines, although they are still the most effective, have problems such as needle-associated pain, risk of contamination, need for trained personnel, and limited acceptance in low-resource settings. Consequently, the recent developments have been focusing alternative, non-invasive platforms, especially oral and transdermal delivery systems.*

Oral vaccines are attractive because they access the mucosal immune system and facilitate mass vaccination; however, they face challenges of enzymatic degradation and variable absorption in the gastrointestinal tract. To resolve these difficulties, emerging technologies such as polymeric nanoparticles, liposomes, and targeted microencapsulation are being utilized. At the same time, transdermal systems, which include microneedle arrays, dissolvable patches, and electroporation-assisted delivery have overcome limitations of injectable vaccines by allowing painless administration, thermostability, and self-application thus, they are highly recommended for pandemic preparedness.

This review article provides an overview of the current innovations, comparative benefits, formulation challenges, and future perspectives in oral and transdermal vaccine delivery systems. It discusses how these novel approaches are facilitating the transformation of global vaccination strategies and opening the door to the next-generation patient-centric immunization platforms..

Keywords: Vaccine delivery systems, oral vaccines, transdermal vaccines, microneedle patches, nanoparticle delivery, mucosal immunity, needle-free vaccination, controlled release, thermostable vaccines.

I. INTRODUCTION

Vaccination is still among the top measures that can be taken to improve public health, yet the traditional use of injection methods in most cases brings about problems of logistics, biology, and even social challenges. For instance, the delivery that depends on the use of a needle usually has to be done by a healthcare professional, while the product needs to be kept in a cold chain and a sterile environment which all together make the vaccines less accessible to people living in areas that are far away from the city or have no proper medical facilities.[9][1] Moreover, the fear, pain, and risk of infection that comes along with the use of a needle may cause the vaccine demand to decrease at the population level.

The drawbacks of vaccines have led to the invention of other routes of delivery that are able to facilitate administration, increase the immune system, and enable universal vaccination coverage. Among the innovations likely to be accepted and recognized as effective are oral and transdermal vaccine delivery systems, which provide a needle-free, user-friendly, and possibly self-administrable platform. Oral vaccines exploit the natural pathways of the digestive system to

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generate strong mucosal and systemic immunity though they have to deal with enzymatic breakdown and differing intestinal absorption.[6][2] The use of nanoparticles, polymeric coatings, and bioadhesive systems as protective carriers is gradually solving the problem of stability and targeted release. At the same time, the transdermal approaches, especially microneedle patches and dissolvable arrays, give the least invasive means to the immunologically rich dermal layers thus fast resulting in antigen presentation with little or no discomfort. In addition to this, these innovations also come with improved thermostability and easy provision which make them greatly useful in the case of pandemics and mass vaccination programs.[6][3][15]

This article brings to light the latest inventions, their features, challenges faced, and future perspectives of oral and transdermal vaccine delivery systems. By putting emerging platforms against conventional ones, the paper demonstrates how the delivery methods of the next generation are changing the face of vaccination all over the world and facilitating the transition to more accessible and patient-centric immunization.[8][5][9]

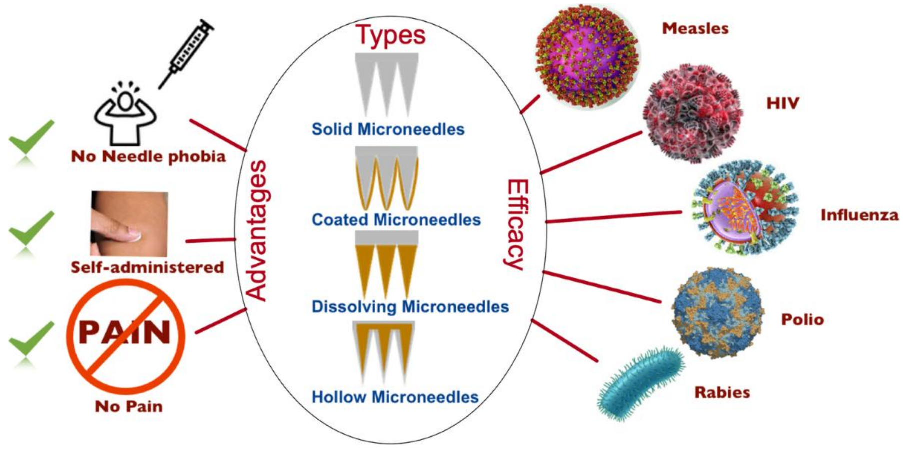

Fig : Types of Microneedles

Advantages of Oral vaccines

Painless and Non-Invasive

Without using needles, pain is removed and the method of vaccination can be accepted by more people, especially children and individuals who are afraid of needles.[9][11]

Induces Strong Mucosal Immunity

Oral vaccines induce IgA-mediated mucosal immunity in the intestine, which is the natural portal of many pathogens such as cholera, polio, and rotavirus.

Easy Administration and Self-Dosing

They can be done by a person himself without the need of a professional, thus they are great for mass vaccination programs.[4][8]

Improved Safety

There are no risks of injuries by the needle, contamination of blood, or throwing away of sharp biomedical waste.

High Compliance and Acceptance Due to their simple use, they are more acceptable to patients, e.g., children and the elderly.

Cost-Effective for Large-Scale Immunization

Reduced need for healthcare workers and a group of injection devices that are essentially sterile.

Better Suitability for Low-Resource Regions

By significantly simplifying the logistics, oral vaccines become handy in case of localities without proper means of transport and in infection situations that cannot be controlled immediately..

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Natural Route of Immunization

In most cases, the immune response generated is more physiologically relevant since the vaccine imitates the natural entry route of the pathogen.

Potential for Mass Campaigns

Due to the quick distribution, it is a good option for emergency immunization during epidemics or pandemics..

Reduced Risk of Cross-Contamination

There are no shared needles, and hence the transmission of blood-borne diseases is at a minimum.[5[[2]

Advantages of Transdernal Route Vaccines

Painless and Minimally Invasive

Microneedle patches and other transdermal systems avoid conventional needles, significantly reducing pain and improving patient comfort.[4]

High Patient Compliance

Easy and convenient to use, making them highly acceptable across all age groups, especially in needle-phobic individuals.

Targets Immune-Rich Skin Layers

The skin contains abundant antigen-presenting cells (APCs), such as Langerhans cells and dendritic cells, enabling strong and rapid immune responses.

Self-Administration is Possible

Transdermal patches can be applied at home without professional assistance, supporting large-scale and decentralized vaccination.[8]

Reduces Need for Cold Chain

Many microneedle formulations exhibit improved **thermostability**, allowing storage at room tempeature and simplifying global distribution.

Lower Risk of Infection and Contamination

No needles means no sharps waste, no needlestick injuries, and a lower chance of cross-contamination.

Dose Sparing Effect

Targeting the dermal immune cells often requires **smaller antigen doses**, making vaccines more economical and valuable during shortages.

Improved Safety Profile

Minimizes systemic side effects and reduces the risk of injection-related complications.

Precise and Controlled Delivery

Microneedle systems can deliver vaccines in controlled amounts, enhancing consistency and efficacy.[22]

Enhanced Stability of Modern Vaccines

Suitable for delivering **DNA, mRNA, and peptide-based vaccines**, which benefit from localized and stabilized delivery.

Simplified Logistics During Pandemics

Easy distribution, self-application, and reduced cold-chain requirements make transdermal patches ideal for emergency vaccination campaigns.[18]

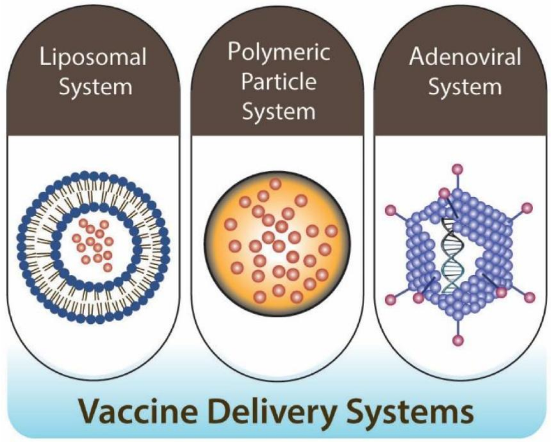

Fig- Vaccine Delivery System

Recent Development in Vaccine Delivery System: From Oral to Transdermal Route

Vaccine delivery systems have changed considerably as scientists are moving beyond the conventional method of injections to create methods that are safer, more effective, and more accessible. The oral and transdermal delivery routes are two of the most potential advancements, in which each of them providing unique advantages and technological innovations.[16[[9]

II. RECENT DEVELOPMENTS IN ORAL VACCINE DELIVERY

2.1. Modern Oral Delivery Technologies

Nanoparticle Carriers

Polymers (PLGA, chitosan) protect antigens from degradation.

Improve uptake through intestinal M cells.

Lipid-Based Formulations

Liposomes, niosomes, and solid-lipid nanoparticles increase stability and control release.

Microencapsulation

Enteric-coated microspheres shield vaccines from stomach acid and release them in the intestine.

Mucoadhesive Systems

Adhesive polymers help vaccines stay longer in the GI tract for better absorption.

Recombinant Live Vectors

Engineered bacteria or viruses that express antigens and stimulate strong immune responses.[15][28]

2.2. Emerging Oral Vaccines

Oral influenza vaccines under clinical studies.

Oral COVID-19 vaccine candidates showing promise for global distribution.

Development of oral vaccines for norovirus, rotavirus, and even cancer therapy.[12]

III. RECENT DEVELOPMENTS IN TRANSDERMAL VACCINE DELIVERY

3.1. Microneedle (MN) Technology

Microneedles have revolutionized transdermal vaccination due to their safety, simplicity, and efficiency.

Types include:

Solid microneedles – create microchannels for enhanced delivery.

Dissolvable microneedles – made from biodegradable polymers that dissolve in the skin.

Coated microneedles – vaccines coated on needle tips for quick release.

Hydrogel-forming microneedles – swell and deliver vaccines in a controlled manner.[21]

3.2. Other Transdermal Innovations

Jet Injectors

– Deliver vaccines using high-pressure liquid streams.

Electroporation Systems

– Use electric pulses to increase skin permeability.

Thermo/Light-Activated Patches

– Patches that release vaccine when heated or exposed to specific light wavelengths.[12]

3.3. Stability & Storage Breakthroughs

Many microneedle patches show **room-temperature stability for months**, reducing cold-chain dependence. Suitable for emergency outbreaks and remote areas.[31][4]

3.4. Applications Under Development

Microneedle-based vaccines for influenza, measles, COVID-19, hepatitis B, HPV, rabies, and DNA vaccines. Growing interest in mRNA delivery via microneedles for painless, targeted immunization.[7][9]

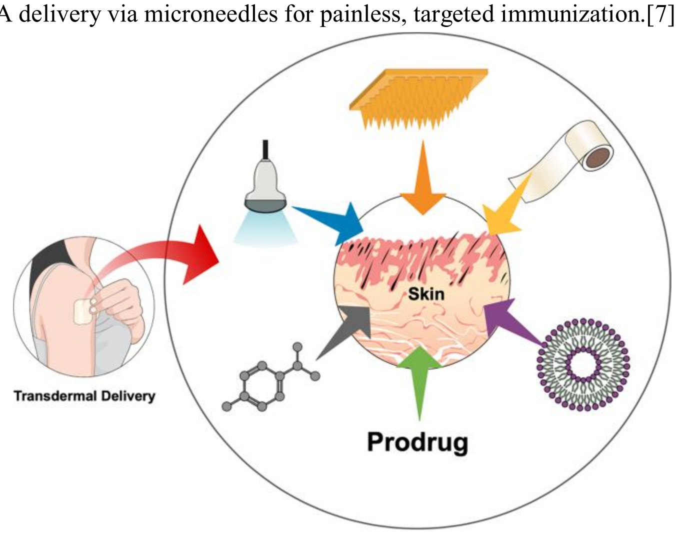

Fig- Transdermal Delivery

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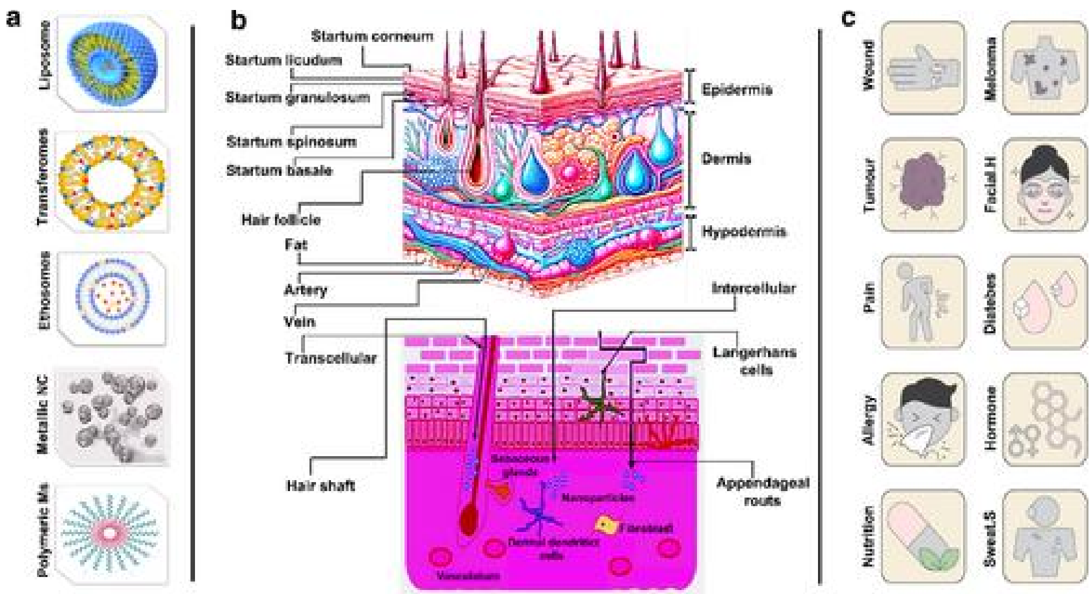

Fig- Working of Transdermal and Oral vaccine on Body

IV. DISCUSSION

The rapid development of oral and transdermal vaccine delivery methods demonstrates a worldwide shift towards more accessible, acceptable, and adaptable immunization strategies than the traditional injection ones. Injectable vaccines are still at the core of immunization programs, but issues such as the fear of needles, cold chain requirements, and the need for trained personnel have led to a significant increase in the interest of alternative delivery routes, particularly in the case of pandemics and mass vaccination. Significant advancements have been made in oral vaccine delivery to protect and uptake antigens with nanocarriers, mucoadhesive polymers, and targeted release systems. These technologies work to eliminate the challenges of gastrointestinal degradation and variable absorption.

However, the complex and highly variable gut environment, which can affect both stability and immune response, still limits oral vaccines. On the other hand, transdermal delivery, especially with microneedle technologies, is a very attractive needle-free option. Transdermal systems, by using fewer antigen doses, achieve strong immune responses as they target the skin's rich network of antigen-presenting cells. Their painless application, better thermostability, and the possibility of self-administration make them, in particular, the next vaccination rounds of large-scale and low-resource vaccination efforts. However, issues related to drug-loading capacity and production uniformity are the challenges that need to be worked on further. Comparative review of the two delivery methods suggests that oral vaccines are more convenient and better at inducing mucosal immunity, whereas transdermal systems allow for delivery that is precise, efficient, and dose-sparing.

As a result, they are not rivals but rather potent complementary strategies targeted at widening vaccine access worldwide. The emergence of oral and transdermal vaccine technologies can be interpreted as a move towards patient-centered and technologically advanced immunization approaches. To realize their full potential and improve global vaccination strategies, further innovation in formulation stability, delivery efficiency, and large-scale production will be needed.

V. CONCLUSION

Recently, oral and transdermal vaccine delivery methods have radically changed the concept of immunization from conventional needle-based to safer, patient-friendly, and readily available approaches worldwide. Oral vaccines are painless and induce strong mucosal immunity, whereas transdermal devices, in particular, microneedle-based systems, offer accurate, dose-sparing delivery with potent dermal immune activation. These novel solutions, in fact, overcome the major obstacles that exist in the use of conventional vaccines such as the need for the cold chain, risks associated with needles, and limited accessibility in economically disadvantaged areas. Ongoing efforts in formulation optimization, scalable manufacturing, and clinical validation will be necessary to unlock their full potential, thereby reshaping global vaccination programs and enhancing pandemic preparedness.

VI. RESULTS

Recent research show significant progress to oral and transdermal vaccine delivery systems, and thus position these two modes as potent alternatives to the current injectable vaccines.

On the oral delivery side, nanoparticles, liposomes, and polymer-based carriers are used to improve antigen stability and uptake in the gastrointestinal tract. Mucoadhesive and enteric-coated formulations have been utilized to overcome the issues of gastric degradation and absorption resuming from the stomach. Established oral vaccines such as polio, rotavirus, and cholera, elicit effective mucosal and systemic immune responses whereas oral vaccines for influenza and COVID-19 are still at the preclinical stage showing promising results. However, oral vaccines are still limited by the variable and complex environment of the gut which may affect their efficacy.

Transdermal vaccine delivery has evolved immensely, especially through microneedle arrays, dissolvable patches, and hydrogel-based systems. Besides, these devices trigger immune responses effectively with small antigen doses by targeting the skin's antigen-presenting cells (APcs), thus they could be used for dose-sparing strategies. In addition, cold-chain logistics, which limit the use of vaccines in remote areas, can be overcome by thermostable formulations that, consequently, transdermal vaccines are perfect for mass immunization programs and developing countries. On the other hand, some setbacks such as the low drug-loading capacity and the need for large-scale manufacturing standardization are still present.

On the one hand, oral vaccines have benefits in terms of ease of use, patient adherence, and mucosal immunity. On the other hand, transdermal vaccines may offer targeted, efficient delivery, strong dermal immunity, and enhanced stability. Ultimately, these breakthrough technologies may help realize the global vaccine accessibility through employing an integrated oral and transdermal delivery strategy to thereby promote vaccination coverage and pandemic preparedness further..

VII. FUTURE SCOPE

The innovations in oral and transdermal vaccine delivery methods open up significant possibilities for the improvement of immunization programs worldwide. Upcoming studies may emphasize on manufacturing personalized vaccines that are in accordance with the immune system of an individual, thus the effectiveness will be higher and side effects will be minimal. As per the expectation, the merger of these devices with the novel vaccine platforms such as mRNA, DNA, and peptide-based vaccines will make them feasible for the use in these types of vaccines only without going beyond them.

Moreover, the invention of thermostable vaccines that do not require cold-chain storage like microneedle patches can make vaccinations accessible to people living in poor and distant areas. This will also allow a quick vaccine rollout during pandemics. The innovations in the delivery systems that are intelligent and self-administered, for instance, sensor-equipped or controlled-release patches, may be able to optimize the vaccination process as well as its monitoring Furthermore, the edible plant-based oral vaccines can be a viable solution that is both scalable and affordable for large-scale immunization programs. The hybrid regimens that involve oral priming and transdermal boosting simultaneously may result in heightened immune responses as well as longer-lasting protection. In summary, these novel approaches to vaccination highlight the importance of patient-centric, safe, and universally scalable vaccination solutions which oral and transdermal delivery systems as key players in the future of public health.

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