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BIODEGRADABLE POLYMER MICRONEEDLES FOR CONTROLLED-RELEASE DRUG DELIVERY

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ABSTRACT

Micro needles are used for NDDS(novel drug delivery system). Needles are one of the recent advances in drug delivery and have been proposed as a novel drug delivery system. The micro needles shape is designed for polymeric micro particles and this may overcome the injection & patches limits. Control release consists of both the functions of drug matrices and needles. These micro needles are strong and larger in size which is inserted in the skin to transfer the drug in order to stimulate nerve, but these needles may not touch deeper layer. When polymer needles are dissolved, it shows disposal of bio hazardous sharps waste after injecting the drug. In mild conditions of this study, the fabrication of micro needles are added with protein drug delivery to form mass production. This study observed that micro needles are inserting into the skin of the humans and doesn't show any pain or sense. The low ratio &pyramides are used to dissolve micro needles when inserted in the skin to show adequate mechanical strength.

Keywords :-Microneedles, TDDS, thermal polymers.

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INTRODUCTION

Pharmaceutical therapy is the clinical medical science. A biopharmaceutical is a drug where the active compounds are extracted from biological substance. The examples of biopharmaceuticals are insulin, DNA and proteins. The significant limits for delivery are involved. The less absorption was shown by oral drug in GIT, liver. While some of the sensitive drugs which contain proteins can live in GIT. Transdermal drug delivery System (TDDS) acts as drug transport on the skin patches. There are many transdermal patches like nicotine, steroids in systemic medicine which applied topically on the skin surface. These nicotine's are used in smoking cessation, and synthetic steroids to control birth. If the TDDS rate is limited by the stratum corneum barrier, few drugs may enters into the skin. The chemical enhancers, electric fields, ultra sound, thermal methods shows higher permeability on skin. Hypodermic needles are effective and acts as delivery vehicle. It having limitations such as

1. Painful delivery
2. Inconvenient
3. Bolus delivery decreases the drug effectively that would benefit from controlled release overtime
4. The trained medical personnels are involved in children and elderly patients.
5. The lack of bio hazardous sharps waste after delivery and mass immunization Scenario faces problems.

The devices are developed for control release compounds. It shows very slow delivery for hours to years. The delivery option was provided by polymer micro needles [1-4].

Microneedles-Newer Technology

Micro needles are used for NDDS (novel drug delivery system). Needles are one of the recent advances in drug delivery and have been proposed as a novel drug

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delivery system. The micro needles shape is designed for polymeric micro particles and this may overcome the injection & patches limits. Control release consists of both the functions of drug matrices and needles. These micro needles are strong and larger in size which are inserted in the skin to transfer the drug in order to stimulate nerve, but these needles may not touch deeper layer. When polymer needles are dissolved, it shows disposal of bio hazardous sharps waste after injecting the drug. The polymers are dissolved in the skin after inserting micro needles to release encapsulated compounds. The benefit of this bio hazardous sharps faces peoblem in developing countries and when used in home. Fabrication process is the limitation for micro needles kept at room temperature. The efficient method is administered by themselves and is used to transfer the antigens into the skin. The polymers are dissolved and allows vaccines over influenza virus.

Properties of Polymers for Microneedles

The micro needles are produced by micro fabrication method involved for TDDS which consists of efficacy, manufacturing cost and safety. The micro needle components are provided by biodegradable polymers for safety, efficacy and low cost mass production.

Safety: Biodegradable polymer needles are degraded in the skin easily. The re use or sudden breakdown in the skin gives encapsulated drugs of control release. These are produced by biodegradable polymers and are approved by FDA approval.

Efficacy: Micro needles are sharp at the tip and gives mechanical strength undergoes penetration withiout breakdown in the skin.

Low-cost mass production: The versatile fabrication technique produces low cost manufacturing production.

Advantages of Microneedles

1. Easy to use
2. Self-administration
3. Bolus delivery and sustained delivery of drugs within the skin
4. The danger should be avoided when improper lack of needle inserted in developing countries or mayused intentionally.
5. Less time is required and expenses of trained clinical personnel are reduced.
6. **Lack of pain**:The TDDS contains a barrier called stratum corneum which is a superficial layer of the skin. Micro needles forms drug delivery channels by entering through the barrier to avoid nerve pain. But when the conventional needles passed this skin layer delivers the drug compound and shows effectiveness to form pain and infection. While the micro needles easily penetrates through the barrier but do not touch nerve endings. This needles are mostly helpful to decrease the pain chances and to transfer the drug on epidermis and to superficial dermis.
7. **Effective response through skin:** Skin acts as the firat immunological defense barrier to avoid injury and is a sensitive organ. The antigens and foreign particles may penetrate the oustside barrier stratum corneum. This may enhances the defense network such as epidermal langherhans cells, antigen presenting cells and dermal dendritic cells. The pharmacological response is enabled by the drugs and may effects administration than traditional drug delivery mmethods. Foreign agents are taken by langherhan cells to produce antigen specific immune response. The vaccines are transferred through skin. The drug is administered by painless method.

Microneedle Properties

1. **Ruggedness**: Microneedles are produced in optimal size. The micro needles shouldn't be more long due to the breakage of the needle before penetrating into the skin.it should be flexible, rigid without buckling while insertion and do not fracture.
2. **Controlled release**: The micro needles must transfer the controlled drug at particular time.
3. **Penetration:** The micro needles passes the drug in particular tissue depth. The micro needles are easily inserted without pain by taking the force 10N and smoothly pushed. It should have sharpness at the tip and must be strong. The fracture may due to the parameters of shape, size, width and length of the needle.

Dimensions of Microneedles

The dimensions of micro needles are depends on different types. Typical micro needle varies in length of 150 to 1500 microns, 50-250 microns in base width, 1-25 microns in tip diameter. The triangle, arrow and rounded shapes of micro needles are available.

Preparation of Microneedles

Using Master Moulds

The PDMS (poly dimethyl siloxane) is poured in the SU-8 master structure to cure them in incubator at 40°C within 12hours. This PDMS is removed from the master. So, this master is used again to make molds.

Using Polymers

For rapid release

Calcein or Texas-Red-labeled bovine serum albumin (BSA) powder was prevented in acetonitrile at 10%w/v solid content and undergoes homogenization for 5min at 10,000 rpm to produce micro particles of the drug. The homogenized particles ranges from 1 to 100 um undergoes filtration at 30um filter. The filtered substance

is transferred by 1um filter. The final solid cake have the particles size of 1 to 30um distributed in acetonitrile. After adding suspension in the micro needle mold of PDMS is kept in vaccum chamber for 5 minsThemould is filled with drug particles that forces the drug suspension in mold cavity and organic solvent undergoes evoparation. The adhesive tape was used to remove particles on the mold surface.

For slower release

a)Preparation of microneedle matrix

Polymers used are,

1. Carboxymethyl cellulose(CMC)
2. Amylopectin
3. Bovine serum albumin(BSA)

Concentrated CMC was heated with 60 to 70°C at ambient pressure or vaccumed at room temperature. While concentrated BSA & amylopectin is heated at 60 to 70°C or at 37°C. Before and after evaporation, measure the solution mass before and after evaporation to form concentration of solute. Measure the concentrated hydro gel viscosity with couette viscometer. The model drug was dissolved by hand to prevent the concentrated hydro gel compound [5].

b)Casting

The concentrated hydrogel molds the micro needles. The hydrogel of 100 to 300mg was kept in conical centrifuge tube on PDMS mold is centrifuged 45° angled rotor at 3000g & 37°C for 2hours to fill the mold cavity of micro needles and then hydrogel is dried. The micro needles are prepared with encapsulated model drugs. Take the hydrogel 8 to 10 mg was dissolved with model drug and fill the micro needle cavity of mold with this mixture. It dry's within 30minutes on centrifugation. The dry tissue paper is used to remove the hydrogel on the mold surface. In order to prepare back layer, pure hydrogel without drug of 100-200mg was poured and leave to dry on the mold. The same two step process was continued to produce micro needles with model drug but only hydrogel along with drug model are performed to produce back layer.

EVALUATION

***In-Vivo* Testing of Microneedles**

The rabbits or mice's or guinea pigs or monkeys or mouses are used in the pre-clinical invivo studies. This study shows safety and toxicity of the compound or device. Mostly two types of animals are used in invivo preclinical studies to show variety of toxicities from micro needles. In this *In vivo* method, micro needles are tested on the hairless mice by inserting or prickling on the tail vein in the laboratory. This method determines the force of the micro needle penetration in the skin. In this invivo method, micro needles of rhodamine B is tested on the mouse tail and anaesthetic given in rabbit ear within the laboratory to perform penetration, bending breakdown force. In this method, the vaccine delivery that is ovalbumin 20ug within 5seconds as protein antigen model was delivered in guinea pig without hair by using micro needles. This method was used for vaccine anthrax delivered in the rabbits by using solid or hollow micro needles.

Applications of Microneedles

Immunization

Immunization programs are mass vaccines, antidotes are applied in minimal medical training in developing countries. In immunization, the ovalbumin as antigen model was analysed by using novel drug delivery system(NDDS) intra cutaneously and contains micro needle arrays coated with antigens. In vaccination, the influenza vaccine or micro needle patches shows immune response which is tested on mouse and delivered IM route and contains micro needle array patch system with coated antigens [6].

Molecular Docking

Micro needles are used to administer impermeable membrane molecule in the cells. Also used in cell biology. The peptides, proteins, olio nucleotide, DNA and other probes are administered to alter the functions of the cell. DN is administered by micro needle arrays into mammals and plant cells to transfer cells.

Treatment of Acne

The acne was mostly treated by the dissolving micro needle patches and results are performed within the use of 24hours. API and GRAS matrix is present in micro needles. This system transfers 100's ugh of API through barrier in the epidermis. This method was also used in cosmetics. Micro needle patch transfers the intra dermal drug delivery system into the skin.

TDDS

The transdermal drug delivery with small drug molecules are delivered through the barrier stratum corneum and doesn't produce nerve sense in the deep tissue by micro needles which are long to penetrate this layer. The absence of pain in the trans dermal drug delivery. The hollow needles are used to administer proteins, medicines, insulin and nano particles to encapsulate the drug. The micro needle arrays are used to puncture the skin to transfer the drug [7].

Target Delivery of drugs

The target drug delivery prevents detrimental effects by delivering systemic drugs into the tissue with the help of micro needles. This method decreases side effects and drug dosage to provide the deliver which shows difficulty in treating. The multi channel silicon needle is micro fabricated to transfer bio active

compounds in the neural tissue are monitored to stimulate the neuron. Micro needles may penetrate the atherosclerotic arteries of vessel wall and normal arteries in the rabbit. Antirestenosis drug is used [8].

CONCLUSION

In mild conditions of this study, the fabrication of micro needles are added with protein drug delivery to form mass production. This study observed that micro needles are inserting into the skin of the humans and doesn't show any pain or sense. The low ratio & pyramides are used to dissolve micro needles when inserted in the skin to show adequate mechanical strength. FDA approved polysaccharides implements this needle and centrifuged in casting method. When the micro needle matrix is dissolved in the skin, then the micro needle patches shows bolus model drug release. When the back layer is loaded, sustained release of needle patches are due to diffusion and backing layer is swollen within the time. In the invivo method, the micro needles administers peptides, insulin and desmopressin, genetic materials such as DNA, plasmids and oligonucleotides and also vaccinations over anthrax and hepatitis B.

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