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Transdermal patch of curcumin: An overview

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Abstract:

This study is done to understand about the transdermal drug delivery system with its advantages and dis advantages with types of transdermal patch and the components need to formulate a patch. Taking curcumin as main constituent which is found in curcuma longa a rhizomatous herbaceous perennial plant belonging to family Zingiberaceae. An attempt will be done to formulate a patch by understanding material and method required to formulate the patch.

Key words: transdermal drug delivery system, patch, curcumin.

1. INTRODUCTION

Over last few decades the great innovation is done over controlled drug delivery system. In current the technology is improved to such level that delivery of drug can be done at constant rate for certain period of time which can be range from a day to a year without any major issue. Oral route is the most common form of drug delivery it has notable advantages including easy administration but also various drawback such as poor bioavailability due to hepatic metabolism and have tendency to produce rapid blood level, and also leading to a need for high or frequent dosing which can be both cost inconvenient and prohibitive. To overcome all this difficulties there was a need for a innovative drug delivery system which can improve safety and efficacy of drug with minimal loss and side effects. Transdermal delivery system is type of control release system which is applied topically in which patch deliver the drug at a constant rate for 24hrs or longer and the other Norplant system tends to release progestin levonorgestel from silicon rubber tubular capsule for several years. This patches are can be prepared in varying size, which can contain one or more drug. This patches allow the pharmaceutical active substance to deliver across skin barrier.

2. TRANSDERMAL DRUG DELIVERY SYSTEM

Drug delivery system (DDS) are methods or technologies that mainly carry the drug into various parts of body. DDS can also be explain on the basis of there type of packaging like micelle or Nano- particle which protect the drug from getting degrading over a period of time and helps to travel wherever it need to go in body.

From thousands of years the human civilization used various substance on skin as cosmetic or medicine for local effect till 20th century, in later 20th century the skin was used as drug delivery route. Routine use of TDDS become common in later third of the 20th century when technology was developed to its fullest. Surface of average adult body is approximately 2 m^2 and have one-third of blood circulation in body. The human skin is partially accessible for the drug delivery. TDDS has become one of the widely invented form of drug delivery system which is used to deliver drug through skin rather than using conventionally direct route of administration that make use of needle based injection. Transdermal delivery represents an attractive alternative to for oral and hypodermic injection.

Transdermal drug delivery system is also known as skin patch or transdermal patch which deliver the drug at a specific dose to the circulatory system. The very first transdermal patch was developed in 1980 namely Transdermal-Scop which contain the drug Scopolamine for the treatment of motion sickness. This transdermal device is mainly the membrane bounded moderated system and study release is maintained for three day periods, this patch was approved in 1981.

TDDS have various advantage over oral drug delivery system in which most significant is it does not pass through GIT due to which there is no issue of loss of drug due to 1st pass metabolism, and drug can easily delivery without the interference of PH, intestinal bacteria, various enzyme and juices present in stomach. TDDS has improved the delivery of many therapeutic drug such as hormonal therapy, treatment of CNS, cardio vascular system and in pain management. They provide release of drug for prolonged period of time, they improve patient compliance and this system are generally inexpensive. As TDDS is an noninvasive method and it have no or minimal pain due to which it is highly safe and convenient to all age group but specially for children and old age people.

3. ADVANTAGES AND DISADVANTAGES OF TDDS

3.1. Advantages

- Inconveniences of IV therapy is avoided
- It avoids the first pass metabolism due to which there is no stage of disintegration and dissolution and drug directly goes into blood stream.
- It gives better patient compliance due to elimination of dose at various interval.
- Easy termination of therapy can be done if any major problem is seen.
- TDDS provide steady plasma level due to which therapeutic index is maintained.
- It provide the steady infusion of drug over an extended period of time due to which multiple dosing is avoided.
- This system is suitable for the drug having short biological half-life.
- Self-administration can be done with easy removal when needed.
- Therapeutic failure or adverse effects frequently associated with intermittent dosing for the chronic disease can be avoided.
- It's an overcome to injection based administration with no or minimal pain.
- Safe parenteral route of administration.

3.2. Disadvantages

- Drug with bigger particle size can't be formulated due to skins low permeability.
- Skin irritation and sensation are be possible.
- Patient trust can be a barrier to effective transdermal therapy.
- TDDS can't deliver drug in pulsatile fashion.
- TDDS can't deliver the ionic drugs through skin.

4. TYPES OF TRANSDERMAL PATCH

There are mainly 4 types to transdermal patch

1. Drug in reservoir

2. Drug in matrix

3. Drug in adhesive

4. Drug in Micro reservoir

4.1. Drug in reservoir

In this types of patch a rate controlling membrane is present between the skin and drug reservoir. For this microporous or dense polymeric membrane can be used. E.g. of materials that can be used as rate controlling membrane – polyester elastomer, ethylene vinyl acetate copolymer, silicones, high density polyethylene. A membrane should have ideal property of being permeable to drug and enhancer and should also retain other formulation excipients. Drug reservoir can be made of various materials ranging from simple to complex formulation. A reservoir should allow the release of zero order drug over delivery period.

4.2. Drug in matrix

In this type the drug is equally dispersed in a polymeric matrix, through which drug diffuses through skin. This matrix is mainly compose of silicon elastomer, polyvinyl alcohol, polyvinyl pyrrolidones, and may be consider as the drug reservoir. The drug get release from a polymeric matric under zero order kinetics, only if drug is maintained at a saturation level in the fluid phase matrix and if its diffusion rate in the matrix is much greater than its diffusion rate in skin.

4.3. Drug in adhesive matrix

This a simplest system in which drug and enhancer are formulated into an adhesive mixture that is coated into a backing membrane to formulate an adhesive tape.

4.4. Drug in micro reservoir

This system is mainly combination of reservoir and matrix dispersion system. To make drug reservoir in this system the drug is suspended in an aqueous solution of water soluble polymer and then the resultant solution is homogenously made to dispersed in a lipophilic polymer to form numerous un leachable, microscopic sphere of drug reservoir.

5. COMPONENTS OF TDDS

1. Polymer matrix
2. Membrane
3. Drug
4. Permeation enhancer
5. Backing lamination
6. Release liner
7. Other excipients

5.1. Polymer matrix

Polymer are the backbone of TDDS they control drug release from the device. This polymer matrix can be made by dispersing drug into a liquid or solid state synthetic polymer base. Mainly the polymer which are compatible with drug and other components of system (like penetration enhancer and PSAs) should be used for this system. Polymer should deliver the drug at constant and effective rate throughout the intended self-life of product, and should be safe. Example of some polymer used for tdds are- natural polymer (cellulose derivatives, zein, gelatin, shellac), synthetic elastomer (hydrin rubber, silicon rubber, nitriles, butyl rubber, neoprene etc.), synthetic polymer (ethylene, polyvinyl alcohol, polyvinyl chloride etc.)

5.2. Membrane

This membrane is sealed to backing layer to form a pocket like structure to enclose the drug containing matrix or is used in single layer in the patch formation. Ethylene vinyl acetate, silicon rubber, polyurethane are used as membrane.

5.3. Drug

Drug is the most important component of tdds. This is the therapeutic agent which is to be deliver through skin so there must be care full selection of the drug. Ideal properties for drug must me

- Molecular weight must be <1000 Dalton.
- Should have affinity to both lipophilic and hydrophilic phases.
- Should have low melting point.
- Should match PH level of skin that is 4.2-5.6.
- Drug should be potent.
- Should have short half-life.
- Drug should be no irritant and non-allergic

Example of drug that can incorporated into TDDS: atenolol, metoprolol, clonidine, carvedilol etc.

5.4. Permeation enhancer

The penetration of drug through the TDDS can be improved to by adding permeation enhancer. This agent mainly increase the permeability of Stratum corneum layer to attain higher therapeutic level of the drug. Permeation enhancer mainly interact with the components of SC layer, and modify the barrier function of layer, thereby leading to increase permeability. There are mainly 3 pathway for drug penetration namely polar, non-polar and polar/nonpolar, and this penetration enhancer alter on of this pathway.

5.5. Backing lamination

Backing layer must impart flexibility, appearance, and occlusion properties to the TDDS. While designing the backing layer the chemical resistance of the material should be consider. The excipients compatibility should also be considered as prolonged contact between the backing layer and the excipients this may result in the leaking of excipients from the backing layer or may good diffusion of excipients or drug penetration enhancer through the layer. The most suitable backing is one which has good flexibility, good oxygen, lowest modules, and high moisture vapour transmission rate.

5.6. Release liner

A protective layer is applied on the patch as a covering during storage period. This liner is removed during the application of patch to skin. This liner must be inert in nature as it remain in intact contact with the patch. Release liner is made of non- occlusive base layer and release coating layer of silicon or Teflon.

5.7. Other excipients

Methanol, acetone, isopropanol, chloroform, dichloromethane, are some example of solvent used for preparing drug reservoir. Triethyl citrate, polyethylene glycol, dibutyl phthalate are some example of plasticizer are used for TDDS release liners.

6. CURCUMIN: ACTIVE PHARMACEUTICAL INGRIENTS

Curcumin is active chemical constitution of turmeric belonging to family zingiberaceae of kingdom plantae obtain from the root of curcuma longa.

Curcumin is a yellow pigment found in turmeric and it's a polyphenol compound. It has incorporate seven carbon chain and three major functional group α, β-unsaturated β-diketone and aromatic O-methoxy-phenolic group.

Curcumin is used as coloring agent since centuries for food coloring purpose and also used in various medical preparation widely used in Chinese and Ayurveda medicine. It also have beneficial pharmacological properties including anti proliferative , anti-oxidant, anti-inflammatory, anticancer, anti-thrombotic, anti-hepatotoxic, anti heumatic, anti-microbial, antiviral, antioxidant, larvividal, carminative, insecticidal, antivenomous, anti tyrosinase etc.

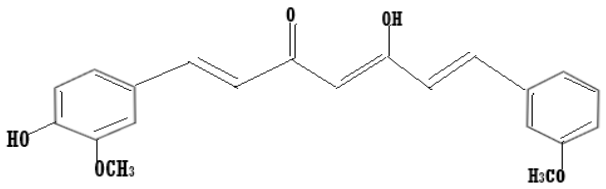

Fig. Structure of curcumin

7. FORMULATION OF TRANSDERMSAL PATCH OF CURCUMIN

7.1. Requirement

API: Curcumin

Chemical: Ethanol, sodium lauryl sulphate, glycerin, distilled water.

Polymer: Hydroxyl propyl methyl cellulose, ethyl cellulose.

Apparatus: Pipette, beaker, standard flask, petri dish, dropper.

7.2. Preparation of standard curve for curcumin

7.2.1. Primary stock solution

Take accurately weighted 100gm curcumin and dissolve it in 30ml of ethanol and dilute to 100 ml of distilled water.

7.2.2. Secondary stock solution

1ml primary solution was diluted to 100ml of distilled water to get concentration of 10mcg/ml. From the above dilution 1ml was pipette out and diluted to 10ml to get concentration of 1mcg/ml. Aliquots of 1ml, 2ml,4ml, 6ml, 8ml, 10ml, were pipette out and dissolve to 10ml of distilled water to get 1mcg,3mcg,4mcg,6mcg,8mcg, and 10mcg concentration of curcumin.

7.3. Preparation of sodium lauryl sulphate solution

500mg of sodium lauryl sulphate was accurately weighted and transfer into 100ml volumetric flask and add distilled water to make up the final volume.

7.4. Preparation of transdermal patch

To make the transdermal patch of curcumin the solvent casting technique is used.

7.5. PROCEDURE

- **Preparation of F1 patch**

Take 1gm HPMC and 1gm EC and dissolve in 10ml of distilled water and 10ml of ethanol respectively.

- **Preparation of F2 patch**

1gm of HPMC and 0.5gm EC and dissolve in 10ml distilled water and 10ml ethanol respectively.

- **Preparation of F3 patch**

-Take 0.5gm HPMC and 1gm EC and dissolve in 10ml distilled water and 10ml ethanol respectively.

-From above every solution mix 9ml HPMC solution and 1ml of EC solution separately. Add 2-3 drops of glycerin to each mixture and mix well.

-Now dissolve 20mg of curcumin in 10ml ethanol and pour it to every mixture with continuous stirring with help of magnetic stirrer.

Pour each mixture into separate petri dishes and allow to stand for 24 hours.

After 24hrs this patches will be ready for evaluation and use.

8. EVALUATION

Following listed approaches should be carried out for study of evaluation

1. Interaction studies
2. Patch thickness
3. Weight uniformity
4. Folding endurance
5. Percentage moisture content
6. Percentage moisture uptake
7. Water vapour permeability
8. Drug content
9. Uniformity of the dosage unit test
10. Shear adhesion test
11. Peel adhesion test
12. Thumb tack test
13. Quick stick
14. Rolling ball tack test
15. Percentage elongation
16. break test
17. Flatness test
18. Polarization examination
19. Probe tack test
20. In vitro drug release studies
21. In vitro skin permeation studies

9. CONCLUSION

Transdermal drug delivery system is a innovate system and advantageous over the needle based injection. It is painless and easy method to deliver the drug into the blood stream without passing through GIT at a pre-determined rate.

Method and material required to formulate the curcumin patch was over viewed by taking HPMC and EC as polymer at various ratio. This curcumin patch formulated need the various evaluation studies mentioned. Curcumin get release by patch and penetrate into skin and get releases for 24 hours. This curcumin present in patch show the anti-inflammatory and anti-oxidant effect.

Overall finding show that limitation of using oral curcumin can be resolve by formulating curcumin in patch especially for inflammatory therapy.

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