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Review On: Transdermal Herbal Drug Delivery System

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ABSTRACT:
Novel herbal drug delivery system opens new wister's for delivery of herbal drugs at right place. At right concentration, for height right period of time. And also gives scientific angle to verify the standardization of herbal drug, several novel herbal delivery systems have been successfully developed in recent year like, liposomes, Phytosomes , solid liquid nanoparticles, ethosomes , micro emulsions and various other vesicular system. Transdermal drug delivery System (TDDS) also known as patches are dosage forms designed to deliver a therapeutically effective amount of drug across a patient Skin. This system is one the very effective ways of delivering drug to the body. These are topically administered medicaments. Transdermal patches are pharmaceutical preparation of varying Sizes, containing one or more active ingredient intended to be applied on the unbroken Skin. The present analysis emphases on the herbal approach in TDDS and eliminating the inconvenience caused in oral route of administration such as, unpleasant taste, odour, colour and side effects like gastric uncertainty. Transdermal drug delivery, offers Controlled release of the drug into the patient, it enables a steady blood level profile, resulting in reduced systemic Side effects and, sometimes, improved efficacy over other dosage forms. TDDS has abundant advantages more than usual. Drug delivery route. It involves penetration. Enhancement technique to improve bioavailability and increase the rang of drug for which topical and transdermal is the viable option To Improve Such character's transdermal drug delivery system (TDDS) was emerged which will improve the therapeutic efficacy and Safety the drug thereby reducing both the size and number of doses. Transdermal patch is an adhesive patch that has a Coating of medicine (drug) that is placed on the skin to deliver specific dose of the medicine (drug) into the bloodstream over the period of time with the view transdermal films incorporating herbal drug Components. This review article provides an overview of types of transdermal patches, method of preparation and its evaluation parameter. The objective and aim of the transdermal drug delivery system is topically administered drug in the form of patches that is delivering the drug in the body through the skin for systemic effect at a predetermined time period .The herbal drugs can be utilized in a better form with enhanced efficacy by incorporating them in modern dosage forms. This can be achieved by designing novel drug delivery systems for herbal constituents.

Key-words-Transdermal, patches, Topical, Drug delivery.

I. INTRODUCTION:

Transdermal drug delivery systems (TDDS), also known as "patches," are dosage forms designed to deliver a therapeutically effective amount of drug across a patient's skin. Several TDDS containing drugs such as clonidine, estradiol, fentanyl, nicotine, nitroglycerine, oxybutynin and scopolamine are available in the United States. In the Drug Quality Reporting System (DQRS), the United States Food and Dione (FDA) has received numerous reports of "adhesion lacking" for transdermal drug delivery systems. In the past few decades' considerable attention has been focused on the development of Novel drug delivery system (NDDS) for herbal drug. The novel carriers should ideally fulfil two prerequisites. Firstly, it should deliver the drug at a rate directed by the needs of the body over the period of treatment secondly, it should channel the active entity of herbal drag to the she of action. Conventional dosage forms including prolonged-release dosage form are unable to meet none of these in Phytoformulation research, developing nano dosage Forms (polymeric nanoparticles and nanocapsules, liposomes, solid lipid nanoparticles. Phytosomes and nano emulsion etc.) have a number of advantages, for herbal drugs, Including

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enhancement of solubility and bioavailability protection from toxicity enhancement. Of pharmacological activity, enhancement of stability Improving.Tissue macrophages distribution, Sustained delivery, protection from physical and chemical degradation, etc. Thus, the rans sized novel drug delivery system of herbal drugs have a potential Future For enhancing the activity and overcoming problems associated with plant medicines. Liposomes, which are biodegradable and essentially non-toxic vehicles, can encapsulate both hydrophilic and hydrophobic, material [1]. The application of novel approaches Can also Improve the efficacy of herbal cosmetic formulations on the human body [2].Herbal drugs are becoming more popular in the modern Variety world for their application to cure of diseases with less toxic effects and better therapeutic imitations effects However, Some of herbal extracts/plant actives like instability in highly acidic ph. metabolism etc. Has led to drug levels below therapeutic concentration in the blood resulting in less or no therapeutic effect. Incorporation of novel 'drug delivery technology to herbal or plant actives minimizes the drug degradation' or presystemic metabolism and serious side effect by accumulation of drugs to the non targeted areas and improves the ease of administration in the paediatric and geriatric patients [3] .Herbs and herbal drugs have created interest among the people by its clinically proven effects in different health problem. Herbal drug therapy for skin disorders has been Utilized for many years. Even our biologically dose primitives, the apes, make herbal Selfmedication [4].Now 'days about 74% of drugs are taken orally and are found not to be as valuable as most wanted. To advance such character's transdermal drug delivery System was emerged. With the creation of current time of pharmaceutical dosage forms, transdermal drug delivery system (TDDS) recognized itself as an important part of novel drug delivery systems Trans-dermal dosage forms, still a costly alternative to conventional formulations, are becoming popular because of their exclusive advantages. Improved bioavailability, controlled absorption, extra uniform plasma levels, painless and reduced side effects easy application and Flexibility of terminating drug administration by simply removing the patch to the skin are some of the potential advantages of transdermal drug delivery [5]. In the past few decades, considerable attention has been focused on the development of novel drug delivery system for herbal drags [6]. Drug delivery through the skin to achieve a systemic effect of a drug is commonly known as transdermal drug delivery and differs from usual topical drug delivery [7]. Herbal drugs are becoming more popular in the modern world for their application to cure variety of diseases with less toxic effects [8].Transdermal Drug Delivery system (TDDS) are. Defined ag self-contained discrete dosage forms which are also known as "patches" [9, 10]. TDDs does not involve passage through the gastro-intestinal tract; therefore, there is no less due to first- pass metabolism, and drugs can be delivered without interference Form PH, enzymes, and intestinal bacteria. In addition, TDDS can be used to control drug release according to usage restrictions, thereby Contributing to the high persistence of this method. Most Importantly , because TDDS is a non-invasive administration method and involves minimal pain and burden on the patient, drugs can be safely and conveniently administered to children of the elderly [11, 12]. A drug to be a model for Formulating as transdermal drug delivery should acquire several Physico-chemical properties, such as short half-life, molecular size should be smaller in order for easy penetration small dose, minimum oral bioavailability, et [13]. Transdermal drug delivery system (TODS) are dosage Form designed to deliver a therapeutically effective dose of drug across a patient's skin [14, 15]. Transdermal drug delivery system (TDDS), also known as patches, are dosage forms designed to deliver a therapeutically effective amount of drug across a patient's skin. In order to deliver therapeutic agents through the human skin for systemic effect, the comprehensive. Morphological, biophysical and physicochemical properties of the skin 'are to be Considered. Transdermal delivery provides a leading edge over injectable and oral routes by increasing patient compliance and avoiding first pass metabolism respectivel [16]. Transdermal drug delivery systems CTDDS) are defined as self-contained, discrete dosage Forms which when applied to intact. Skin, deliver the drugs (6), through the skin, at a controlled rate to systemic circulation. The transdermal route of administration is recognized as one of the potential routes for the local and systemic delivery of drugs [17]. To solve this problem, various novel TDDs techniques have been intensively developed and have emerged as attractive administration methods. In addition, such development could represent a competitive advantage over other drag administration methods in terms of the delivered dose, cost-effectiveness, and therapeutic efficacy [18, 19]. Transdermal

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delivery not only provides controlled, Constant administration of drugs, but also allows Continuous input of drugs with short biological 1. Half-lives and eliminates pulsed entry into systemic circulation, which often causes undesirable side effects [20]. The first transdermal system, Transdermal scope was approved by FDA in 1979 for the prevention of nausea and vomiting associated with travel. Most transdermal patches are designed to release the active ingredient at a zero-order rate for a period of several hours to day's following application to the skin. This is especially advantageous for prophylactic therapy in chronic conditions [21].

1.MECHANISM OF ACTION :

A transdermal patch acts as principal carrier of a drug, where it holds it. At the point of administration, adhesive locks the patch to the skin. This allows the patch to stick to the surface and drug release can take place [22, 23].

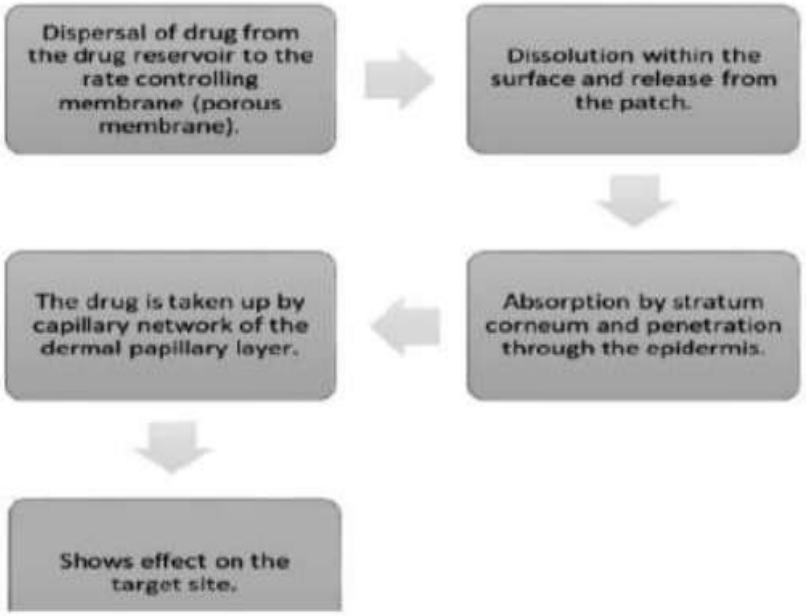
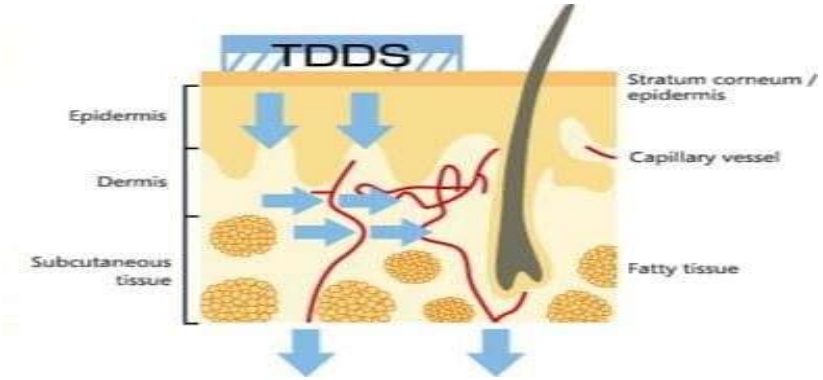


Fig 2- Mechanism of action of transdermal patch



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2.Transdermal Drug Delivery of Herbal Products :

With the passing time, we have come across many deadly diseases and in order to manage and treat it, we have immensely developed synthetical drug, they are useful in curing the diseases however, they come with come with many side effects therefore, herbal approach is a safer mode of treatment comparatively [24]. The transdermal drug delivery system (TDDS) is an innovative drug delivery technique that overcomes the limits of conventional drug delivery systems. Our country has a treasure of Ayurvedic expertise, which has only recently been recognized and created. However, the device for drug delivery is used to give the herbal remedy to the affected patient is old and ineffective, resulting in the drug's potency being limited. As transdermal drug delivery technique is used in herbal medicine, it has the potential to improve the potency and reduce the side effects of a variety of herbal medicines and herbs [25]. To address the fact that about 90% of medications are taken through the mouth and do not exhibit adequate efficacy in comparison to their cost, the TDDS (transdermal drug delivery system) is used as an alternative. High bioavailability, controlled absorption, enhanced plasma level and half-life, painless, safe to use with minimal side effects, and the simplicity of ending drug administration by quickly withdrawing the patch from the skin are only a few of the possible benefits of transdermal drug delivery system [26-27]. The utilization of herbal sources has boosted worldwide In current time, because of their excellent healing properties and almost zero side effects. However, formulating herbal drugs need some modification to deliver the right amount of API by sustained and controlled drug release. The oral route has a variety of additional concerns, including an undesirable taste, odour, and colour. Taking pills causes a slew of additional issues, and as a result, complications arise during recovery. Patients may become disobedient at times. The medications in TDDS patches are continuously released, meaning they have an exact time of action, and the transdermal patch is a non-irritating and non-invasive procedure. For systematic drug administration, it is an appealing contrast to conservative approaches [28]. Transdermal drug delivery system is where a drug is delivered across the skin to have a systemic effect, as opposed to traditional topical drug delivery [29]. The detailed morphological, biophysical, and Physico-chemical Properties of the dermal layer must be addressed when delivering therapeutic agents across the human dermal layer for systemic effects. The transdermal drug delivery system has the most notable benefit over oral and injectable drug delivery in terms of preventing first-pass metabolism and increasing patient compliance [30]. Transdermal drug delivery systems are self-contained, discrete dosage types that, when added to healthy skin, distribute the medication to systemic circulation at a regulated and controlled rate. Transdermal delivery not only allows for controlled, consistent drug administration, it also allows for continuous input of medications with limited biological half-lives and prevents pulsed entry into systemic circulation, which may result in unwanted side effects. As a result, different types of novel and innovative drug delivery systems appeared, such as transdermal drug delivery systems, controlled and predetermined release systems, and transmucosal delivery systems [31,32]. The following table no 1.0 include various herbal approach for the treatment of different disease by using some herbal medication.

3. ANATOMY AND PHYSLOGY OF SKIN :

Skin is the most extensive organ of the body covering under area of about 2m2 on in an average human adult. This multi-layered organ receives approximately one third of all blood circulating through the body. With thickness of only a millimeter, the skin separates the underlying blood circulation network from outside environment .

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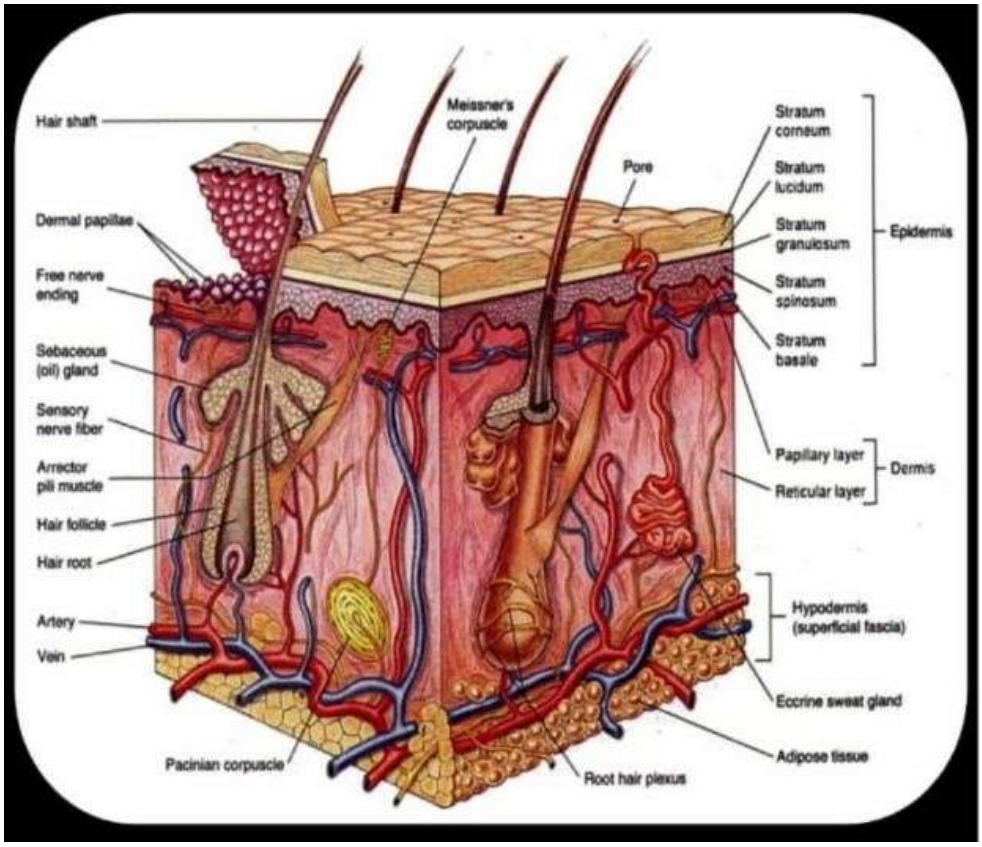

Skin composed of three main layers:
1.Epidermis
2.Dermis
3.Hypodermis

3.1.Epidermis

It is the squamous, stratified, keratinized epithelial layer (20-200 µm thick). It can produce yellow and brown black pigment melanin which contributes color, and absorb UV light. Microscopic sections of the epidermis show two main parts: the Stratum Corneum (SC) and the stratum germinativum. The stratum corneum is the outer most Horney, very thin layer and consists of compacted flattened, dehydrated, keratinized cells in stratified layer. It can resist over 80% of skin permeability. It also consists of nearly non-permeable cornified cells called corneocytes. Keratinized layer of skin is responsible for keeping water in the body and other harmful chemicals out which making skin natural barrier for infection .

Stratum Lucidum is the additional thin layer of keratinized cells which are located beneath the stratum corneum, Mainly present on the palm of hand and on feet soles.

Stratum Granulosum, is a layer where keratinization begins. In this layer, lamellar granules appear and merge with the cell membrane, and these cells release glycophospholipids into intercellular space that forms the main constitute of the water permeability barrier.

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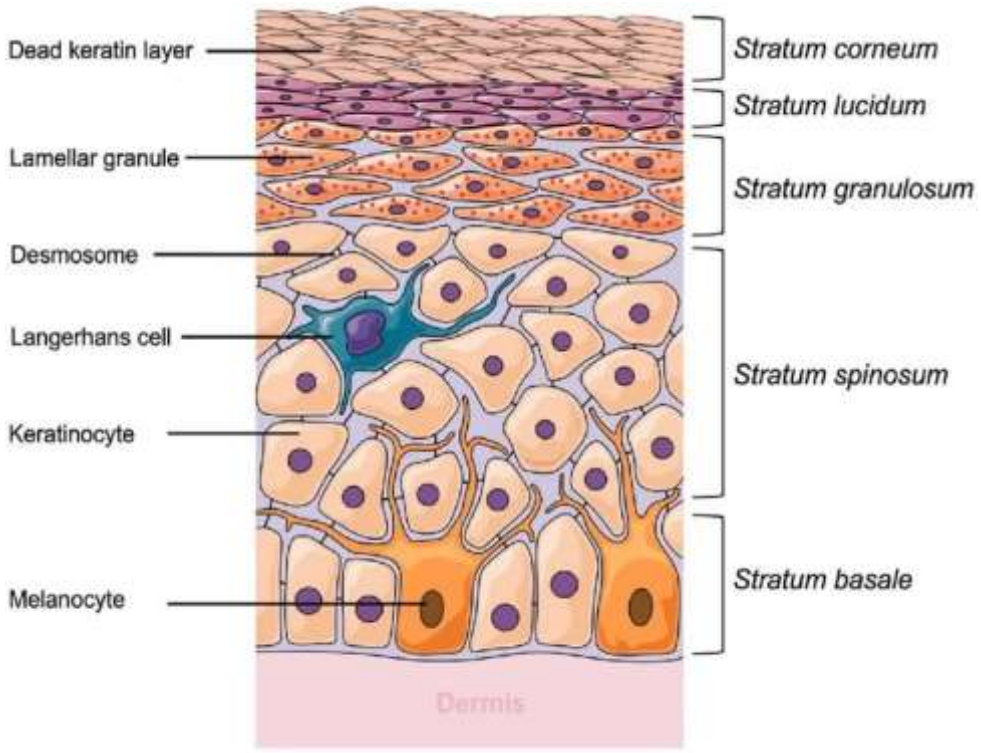

Stratum Spinosum, the spinous cell layer of the skin composed of keratinocytes with a characteristic "prickly appearance due to the presence of desmosomes, important structural filament called cytokeratin.

Stratum Basaleis a continuous single layer consists of columnar epithelial cells also called basal layer or stratum germinativum. It consist of Melanocytes, Langerhan and Merked cells [33].

3.2.Dermis:

It is composed of connective tissues connected tightly to epidermis by a basement membrane.

It consists of hair follicles, sweat glands, sebaceous gland, lymphatic vessels, and blood vessels. The blood vessel in dermis provides nourishment and waste removal from its own cells. It is responsible for biochemical and biological degradation of material transported across lo. Beneath the dermis, the fibrous tissue opens out and merges with the fat-containing subcutaneous tissue [34].

3.3.Hypodermis:

The hypodermis or subcutaneous fat tissue supports the dermis and epidermis. It serves as a fat storage area. This layer helps to regulate temperature, provides nutritional support and mechanically protection. It carries principal blood vessels and nerves to skin and may contain sensory pressure organs. For transdermal drug delivery, drug has to penetrate through all these three layers and reach into systemic circulation while in case of topical drug delivery only penetration through stratum corneum is essential and then retention of drug in skin layers is desired [35].

4.FACTORS AFFECTING TRANSDERMAL PERMEATION:

The factors that affect the permeability of the skin are classified into following three categories:

A. Physicochemical properties of the penetrant molecule
B. Physicochemical properties of the delivery system
C. Physiological and pathological condition of the skin

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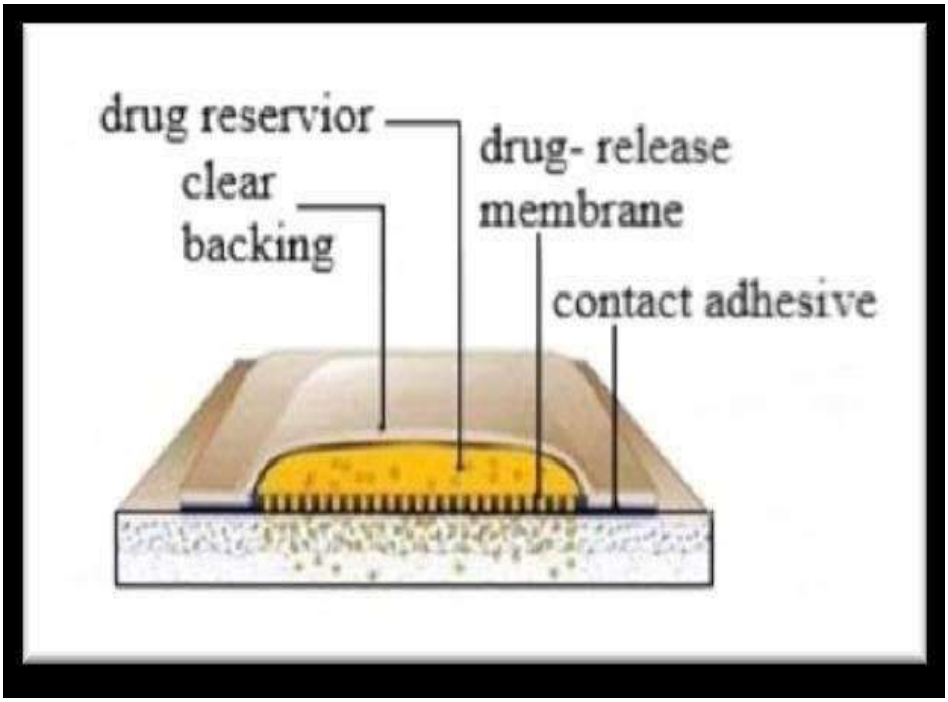

- **Physicochemical properties of the penetrant molecule:**
- Molecular size and shape
- Partition co-efficient
- PH condition
- Ionization
- Drug concentration

Physicochemical properties of the drug delivery system:

- The affinity of the vehicle for the drug molecules
- Composition of drug delivery system
- Enhancement of transdermal permeations

Physiological and Pathological condition of the skin:

- Skin age
- Lipid film
- Skin hydration
- Skin temperature
- Cutaneous drug metabolism
- Species differences
- Pathological injury to the skin
- Blood flow
- Skin metabolism :[36, 37].

5.POLYMER MATRIX/DRUG RESERVOIR

The polymers used for TDDS can be classified as:

1. The Natural polymers: eg. cellulose derivatives, zein, gelatine,Starch and chitosan etc.
2. Synthetic elastomers.

eg. polybutadiene, hydrin rubber, Polyisobutylene, silicon rubber, nitrilbutylrubber etc.

3. Synthetic polymers:

eg. polyvinyl alcohol, Polyvinylchloride, polyethylene, polypropylene, epoxy. polyacrylate, polyamide, polyurea, polyvinylpyrrolidone, polymethylmethacrylate, hydroxypropylcelluloseetc [38, 39].

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Table 1: List of Polymers used in Transdermal Drug Delivery System

Polymer	Type of System
EthylCellulose T-50	Matrix
BIO PSA	Adhesive in Matrix
Scotch Pak	Backing/Release Liner
Eudragit	Matrix
MDX -4-421 (a silicone)	Matrix
Acrylic PSA emulsion	Drug-in-adhesive
Acrylic adhesives	Drug-in-adhesive
Polyisobutylene solutions(Vistanex LM-MH, Vistanex MML-100)	Drug-in-adhesive
Silicone PSA	Drug-in-adhesive
Silicone Oil	Resevoir
EVA	Membrane
Polyisobutylene	Adhesive
ScotchPak 1006	Backing Film
2-Ethylhexyl acrylate	Drug-in-adhesive
Acrylic acid copolymer	Matrix
PIB	Matrix
MDX4-4210 silicone elastomer	Matrix
Acrylate copolymer (Gelva-737)	Matrix
Silicone-2920 and 2675	Matrix
2-Ethylhexyl acrylate and acrylic acid copolymer	Drug-in-adhesive

6.METHOD OF PREPARATION

6.1) METHOD OF PREPARING TRANSDERMAL PATCHES:

Method of preparation of TDDS was summarized by modifying the earlier reported methods.

The patches were prepared by solvent casting method. The polymer (for example PVP/HPMC) was taken in a beaker with a minimum quantity of the solvent. Then 2/3 of the solvent was mixed with the other polymers (for example PVA) and was added firstly with stirring at lower rpm and later at a higher speed. The plasticizer was added and homogeneously mixed and the drug was included with enduring agitation and the volume was made up. The films were cast onto a suitably designed and fabricated glass mould and then dried in oven at 40°C. The films were removed by using sharp blade by inserting along the edges of the film. The dried films were wrapped in butter paper and stored in a closed container away from light [40].

6.2) Asymmetric TPX membrane method:

A prototype patch can be fabricated by a heat sealable polyester film (Type 1009, 3m) with a

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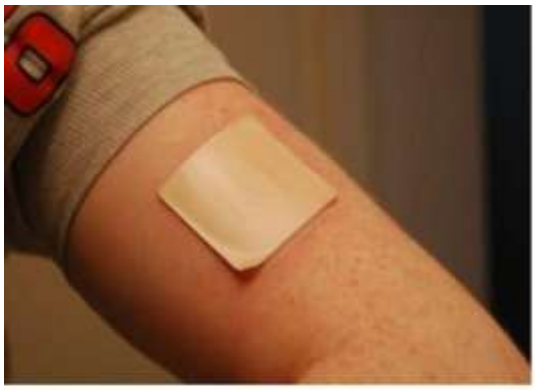
concave of 1cm diameter used as the backing membrane. Drug sample is dispensed into the concave membrane, covered by a TPX (poly (4-methyl-1-pentene)) asymmetric membrane, and sealed by an adhesive.

6.3) Mercury substrate method:

In this method drug is dissolved in polymer solution along with plasticizer. The above solution is to be stirred for 10-15 min to produce a homogeneous dispersion and poured in to a leveled mercury surface. Then the solution is covered with inverted funnel to control solvent evaporation [41].



7. EVALUATION PARAMETERS

7.1) Thickness of the patch

The thickness of the drug loaded patch is measured in different points using a digital micrometer and this determines the average thickness and standard deviation for the same to ensure the thickness of the prepared patch [42].

7.2) Weight uniformity

The prepared patches are to be dried at 60°C for 4 h before testing. A specified area of patch is to be cut in different parts of the patch and weighed in digital balance. The average weight and standard deviation values are to be calculated from the individual weighs [43].

7.3) Moisture content

The prepared films are weighed individually and kept in a desiccators containing calcium chloride at room temperature for 24 h. The films are weighed again after a specified interval until they show a constant weight. The percent moisture content is calculated using following formula.

Moisture content initial weight – Final weight final weight x 100

7.4) Percentage moisture uptake

The weighed films are to be kept in a desiccator at room temperature for 24 hours containing saturated solution of potassium chloride in order to maintain 84% RH. After 24 hours the films are to be reweighed and determine the percentage moisture uptake from the below mentioned formula [44].

Percentage moisture uptake[Final weight – initial weight/initial weight]100

7.5) Drug content

A specified area of patch is to be dissolved in a suitable solvent in specific volume. Then, the solution is to be filtered through a filter medium and the drug content analyzed with the suitable method (UV or HPLC technique). Then, the average of three different samples is taken [45].

7.6) Formulation analysis

Evaluating the physical and chemical properties of the formulation, such as PH viscosity.

7.7) Stability studies

Stability studies were conducted according to the international Conference on Harmonization (ICH) guidelines by storing the TDDS samples at 40 plus/minus 0.5 deg C and (75 plus/minus 51% RH for 6 months. The samples were withdrawn at 0, 30, 60, 90 and 180 days and analyzed suitably for the drug content [46].

8.Future aspects :

During the past decade several theories has been put forktard in addressing the combinations of chemicals and lontophoresis; chemicals and electroporation chemical and ultrasound: iontophoresis and ultrasound; electroporation and iontophoresis; and electroporation and ultrasound Two of the better-known technologies. Significant skin IontophoresisTonotophoresis current permeation that can help achieve enhancement are and photospheres, sonophoresisi. Involves between two passing a direct electrical electrodes Surface. In various devices and TDDS,, drugs can be delivered through the skin to the systemic circulation, rugs are generally reliably and safely delivered through TODS and are safe and stable from biochemical modifications until they reach the target tissue. The TDDS technology is growing rapidly in the pharmaceutical field and has succeeded in capturing key valve in the market for biomedical applications as a formulation system that can

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improve drug. Delivery through topical routes.Active transport methods using external devices has more extensively increase transport of transdermal delivery efficiency of drugs and macromolecules, in recent years. The scale of TODS in the domestic and overseas drug delivery system market has increased, as confirmed through increasing research studies, patents, and commercially available Products from many companies and research institutes. Advances in these TDDSS could provide the driving force for Controlling prevalence of disease & of cardiovascular and central nervous system, diabetes, neuromuscular diseases, genes diseases and infectious and localized infectious diseases, While spearheal spearheading advances in vaccination and Supporting patient preference for selfadministration of drugs for long-term treatment.

II. CONCLUSION /DISCUSSION:

This article provides information regarding the drug delivery process. Systems and an valuable transdermal it's evaluation The foregoing shows that TDDS have great use for active drug. Have potentials, being both hydrophobic able to and hydrophilic substance into promising Transdermal been used as deliverable drug delivery systems Safe drug delivery system devices. Patches prepare different methods these components Of the going patches OF TODS, TDDS, many on incorporate in the arm and effective Transdermal used to by using basic Due to large advantage new researches present newer drugs day to Via the system.

REFERENCE:

[1]. Medina op, zhu Y, kailemok. Carr pharm Des 2004: 10:29.81-9
[2]. Chanchal D. Sklarniata S.J cosmet. Dermatol 2008:9:89-95
[3]. Goyal A; kumar,s. Nagpal M. Singh I, Arora S. potential of novel drug delivery systems for herbal drugs. Ind I pharm Eda Res. 2011;45(3):225-35
[4]. Benzie TFF, Wachtel. Galor S. Herbal medicine: Biomolecular and clinical Boca. Raton (FL): CRC Aspects and edition press: 2011.
[5]. Ahmed A karki N, Charde R, sharde M, Ganghare B. Transdermal Drag Delivery system an overview. IntJBiomedAduRe's 2011; 2:38-56
[6]. saraf As. Applications of novel drug delivery Sistem for herbal formulations. Fitoterapia 2010:81:680-9.
[7]. Yadavsk, Mishra ul, vamshi kJ. Formation and "Evaluation of Transdermal patch for Ayurvedic Medicine Using Different Polymers compositions: In vitro. J Global Trends Pharm sci 2013;4:999-1006
[8]. Bhokaresa, Dongaonkar cc, Lahanesu. Salunke PB, Sawalevs and Thombare Ms, Herbal Novel Drug Deliver: A Review World Joumal of Pharmacy and pharmaceutical sciences., 2016; 5(8):593-611
[9]. Bhowmik D. chiranjib, chandira M, Jajakar B, sampathkp. Recent advances in transdermal drug delivery system. Int. J Pharm Tech Res. 2010:2(1):68-77.
[10]. kumar A, pullankaridam N. Prabhu SL, Gopal v. Transdermal drug delivery systems: an overview. Ant. J Pharm sci. Review Res. 2010; 3(2): 49-54
[11]. Akhter N, singh V, Yusuf M, khan RA. Non-invasive drug delivery technology: development and current status of transdermal drug delivery devices, techniques and biomedical applications. Biomed Tech. 2020:65(3): 243-72. https// dolorg/10.15 is /bmt20190019
[12]. Ruby Pk, Pathak SM, Aggarwal D. critical attributes of transdermal Drug delivery system (TDDS) a generic product development review. Drag DevInd pharm. 2014;40(11): 1421-8. https //dolorg/10.3109/03639045.2013.879720.
[13]. Mishra, B., &Bonde, G.V. (2020), Transdermal drug delivery. In Controlled Drug Delivery systems (PP. 239-275) CRC Press.
[14]. kumar JA, Pullakandam N, prabu SL, Gopal v. Transde- rmal drug delivery system: An overview. Int J pharmasci Rev Res 2010; 3(2):49-53
[15]. Jain NK. Advances in controlled and novel drug delivery. 1 Ed. CBS, publishers and Distributors, New Delhi, 2001: 108-110
[16]. Loyd v. Allen Jr. Nicholas G. Popovich, Howard c. Ansel Pharmaceutical dosage Forms and drug delivery systems, 8th Edition., Wolterkluwer Publishers, New Delhi,2005 PP. 298299.
[17]. selvam RP, singhAk, sivakumar T. Transdermal drug delivery systems fo

Antihypertensive drugs – A review Int J pharm Biomed Res. 2010:1(1):1-8.

[18]. Pawar PM, Solanki KP, Mandali VA Recent advance-ments in transdermal drug Delivery system Int I Phaimelin Res. 2018; 10(3):65-73

[19]. kalkat s, singh R. Rani P. A review on transderma drag delivery snnoriginalInt J sci. 2016;3(4):1-9.

[20]. kumar A, Pullankandam N. Prabhu SL, Gopal v. Transdermal drug delivery system: an overview. Int. J Pharm sci. Review Res, 2010; 3 (2): 49-54.

[21]. Topical and transdermal drug delivery: what a pharmacist needs to know.Inetce. 1" Ed., Arizona: 2004: 1-10

[22]. Qindeel, M., Ullah, M. H., Ahmed, N., &Rehman, A. (2020). Recent trends, challenges and future outlook of transdermal drug delivery systems for rheumatoid arthritis therapy. Journal of Controlled Release. 10;327:595-615. Doi: 10.1016/j.jconrel.2020.09.016.

[23]. Jain SK, Chourasia MK, Sabitha M, Jain R, Jain AK, Ashawat M, JhaAK.DrugDeliv. 2003 Jul-Sep;10(3):169-77. Doi: 10.1080/713840400.

[24]. Barros, N. R. D., Miranda, M. C. R., Borges, F. A., Gemeinder, J. L. P., Mendonça, R. J. D., Cilli, E. M., &Herculano, R. D. (2017). Natural rubber latex: development and in vitro characterization of a future transdermal patch for enuresis treatment. International Journal of Polymeric Materials and Polymeric Biomaterials, 66(17), 871-876. https://doi.org/10.1080/00914037.2018.1506984.

[25]. Ahsan, A., Tian, W. X., Farooq, M. A., & Khan, D. H. (2020). An overview of hydrogels and their role in transdermal drug delivery. International Journal of Polymeric Materials and Polymeric Biomaterials, 1-11. https://doi.org/10.1080/00914037.2020.1740989

[26]. Defraeye, T., Bahrami, F., & Rossi, R. M. (2021). Inverse mechanistic modeling of transdermal drug delivery for fast identification of optimalmodel parameters.Frontiers in Pharmacology, 12, 442.https://doi.org/10.3389/fphar.2021.641111

[27]. Mohammed, Y. H., Moghimi, H. R., Yousef, S. A., Chandrasekaran, N. C., Bibi, C. R., Sukumar, S. C., … & Roberts, M. S. (2017). Efficacy, safety and targets in topical and transdermal active and excipient delivery.In Percutaneous Penetration Enhancers Drug Penetration Into/Through the Skin (pp. 369-391). Springer, Berlin, HHeidelberg

[28]. Mishra, A., & Pathak, A. K. (2017). Plasticizers: A vital excipient in novel pharmaceutical formulations. Current Research in Pharmaceutical Sciences, 7(1), 1-10. DOI: 10:24092/CRPS.2017.070101

[29]. Zhu, J., Tang, X., Jia, Y., Ho, C. T., & Huang, Q. (2020). Applications and delivery mechanisms of hyaluronic acid used for topical/transdermal delivery-A review. International journal of pharmaceutics, 578, 119127.Doi: 10.1016/j.ijpharm.2020.119127.

[30]. Otterbach, A., &Lamprecht, A. (2021). Enhanced Skin Permeation of Estradiol by Dimethyl Sulfoxide Containing Transdermal Patches.Pharmaceutics, 13(3), 320.Doi: 10.3390/pharmaceutics13030320.

[31]. Jasti, B. R., Abraham, W., & Ghosh, T. K. (2021). Transdermal and Topical drug delivery systems. In Theory and practice of contemporary pharmaceutics (pp. 423-454). CRC Press

[32]. Mishra, S., Bishnoi, R. S., Maurya, R., & Jain, D. (2020). Boswelliaserratarox.–a bioactive herbs with various pharmacological activities. Asian journal of pharmaceutical and clinical research, 13(11), 33-39.Https://doi.org/10.22159/ajpcr.2020.v13i11.39354.

[33]. Barry B W; "Dermatological Formulations: Percutaneous Absorption". Drugs and pharmaceutical sciences, Volume-18, Marcel Dekker, Inc. 1983; 1-39

[34]. Mathur V, Satrawala Y, Rajput MS. Physical and Chemical Penetration Enhancers in Transdermal Drug Delivery System. Asian Journal Of Pharmacy 2010, 4 (3),173-183

[35]. Sachan R, Bajpai M, Transdermal Drug Delivery System: A Review, International Journal Of Research and Development in

Pharmacy and Life Sciences, 3 (1); 2013: 2278-0238.

[36]. Arunachalam, M. Karthikeyan, D. V. Kumar, M. Prathap, S. Sethuraman, S. Ashutoshkumar, and S. Manidipa. "Transdermal Drug Delivery System: A Review," Current Pharma Research, Vol. 1, No. 1, Pp. 70-81, 2010.

[37]. Bala P, Jathar S, Kale S, Pal K, Transdermal Drug Delivery System (TDDS)- A Multifaceted Approach For Drug Delivery, Journal Of Pharmacy Research, 8 (12); Dec.2014: 1805-1835

[38]. Aggarwal G, and Dhawan S. Development, fabrication and evaluation of transdermal drug delivery system A review.Pharmainfo.net. 2009.

[39]. Brannon-Peppas Lisa.(1997). Polymers in controlled drug delivery. Medical Plastics And Biomaterials Magazine [Online]. Available http://www.devicelink.com/mpb/archive/97/11/003.html on 10/31/2008).(Accessed on 10/31/2008).

[40]. Shrivastava D. Transdermal Approach of Antidiabetic Drug Glibenclamide: A Review. W J Pharm PharmaSci. 2012; 1: 532-544.

[41]. Arunachalam A, Karthikeyan M, Kumar Vd, Prathap M, Sethuraman S, Ashutoshkumar S, Manidipa S. Transdermal Drug Delivery System: A Review.CurrentPharma Res. 2010; 1(1):70-81.

[42]. Wade A, Weller PJ. Handbook of pharmaceutical Excipients. Washington, DC: American Pharmaceutical Publishing Association, 1994: 362-366.

[43]. Reddy RK, Muttalik S, Reddy S. (2003). Once daily sustainedrelease matrix tablets of nicorandil: formulation and in vitro evaluation. AAPS. Pharm. Sci. Tech.;4: 4

[44]. Janardhanan B, RamachandraPurapu V, Rajappan M, Thengungal pappy R and Probal Kumar M, Formulation development and in vitro and in vivo evaluation of membranemoderated transdermal systems of ampicillin sodium in ethanol: pH 4.7 Buffer solvent system. AAPS PharmSciTech.8 (1);2007: E1-E6.

[45]. Shaila L, Pandey S, Udupa N. (2006). Design and evaluation of matrix type Membrane controlled Transdermal drug delivery system of nicotin suitable for use in Smoking cessation. Indian.Journ. Pharm sci. 68:179-84.

[46]. .Singh J, Tripathi KT, Sakia TR. (1993). Effect of penetration enhancers on the in vitro Transport of ephedrine through rate GSkin and human epidermis from matrix based transdermal