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Comprehensive Review on Transdermal Drug Delivery System

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ABSTRACT :

Transdermal drug delivery systems (TDDS) have emerged as a promising avenue for efficient and patient-friendly drug administration. This review explores the key advantages and applications of TDDS in modern pharmaceutical practice. By providing a non-invasive and convenient alternative to traditional routes of drug delivery, TDDS ensures controlled and sustained release of medications, thereby maintaining stable plasma levels and minimizing fluctuations in drug concentrations. This approach not only enhances therapeutic efficacy but also reduces the risk of gastrointestinal side effects and hepatic degradation associated with oral administration. TDDS exhibits versatility in accommodating a wide range of therapeutic agents, including small molecules, peptides, and large biologics, thereby expanding treatment options across various medical conditions. Additionally, advancements in formulation technologies hold promise for personalized medicine approaches, allowing for tailored drug delivery based on individual patient needs and pharmacokinetic profiles. Overall, TDDS represents a valuable tool in modern pharmaceuticals, offering improved patient compliance, enhanced bioavailability, and the potential for optimized therapeutic outcomes.

INTRODUCTION

Transdermal drug delivery systems are innovative pharmaceutical formulations designed to administer drugs through the skin for systemic distribution. Unlike traditional routes of administration like oral ingestion or injection, transdermal delivery offers several advantages such as non-invasiveness, avoidance of first-pass metabolism, and sustained release kinetics. This route is particularly beneficial for drugs requiring continuous or controlled release over an extended period.

Transdermal patches are the most common form of transdermal drug delivery systems. These patches are typically composed of multiple layers, each serving a specific function in drug delivery. Upon application to the skin, the patch delivers the drug, which then permeates through the skin layers and enters the bloodstream, exerting its therapeutic effects.

The design of transdermal patches involves careful consideration of factors such as drug physicochemical properties, skin permeability, and patch adhesive properties. Additionally, factors like skin integrity, thickness, and blood flow at the application site influence drug absorption rates.

Transdermal drug delivery systems offer several advantages, including improved patient compliance due to ease of use, reduced side effects associated with fluctuations in drug plasma levels, and potential for controlled drug delivery. However, they also present challenges such as limited drug permeability through the skin barrier and variability in skin properties among individuals.

Overall, transdermal drug delivery systems represent a promising approach to drug administration, offering a convenient and effective alternative to traditional routes of delivery. Continued research and development in this field aim to overcome existing limitations and further enhance the therapeutic potential of transdermal formulations.

ADVANTAGES:

- Avoid first-pass gastrointestinal and hepatic metabolism.
- Ensures consistent absorption control.
- Fewer side effects
- Reduce exposure to unwanted metabolites.
- Patient compliance with treatment increases because the drug does not need to be administered multiple times.
- Increased therapeutic effect.

- Easy to apply and remove.
- Non-invasive and painless.
- self care.
- Effective for drugs with short biological half-life and narrow therapeutic window.
- If an adverse reaction occurs, the dispenser can be easily removed.

LIMITATION OF TDDS:

- **Limited Drug Types**: Not all drugs can be effectively delivered through the skin. Only drugs with specific physicochemical properties, such as being small, lipophilic, and having low molecular weight, are suitable for transdermal delivery.
- **Skin Barrier**: The stratum corneum, the outermost layer of the skin, acts as a barrier to drug penetration. This barrier limits the types of drugs that can be delivered transdermally and the rate at which they can be absorbed.
- **Rate of Absorption**: Transdermal drug delivery tends to be slower compared to other routes such as oral or intravenous administration. This limits the usefulness of transdermal patches for drugs that require rapid onset of action.
- **Skin Irritation**: Some drugs or components of the transdermal patch can irritate the skin, leading to local reactions such as redness, itching, or rash.
- **Size Limitation**: The size of the drug molecule can limit its ability to penetrate the skin. Large molecules may not be able to pass through the skin barrier effectively.
- **Dose Limitation**: Transdermal patches have a limited capacity to deliver high doses of drugs. The size of the patch and the rate of drug release can restrict the amount of drug that can be administered transdermally.
- **Patient Compliance**: Transdermal patches require proper application and adherence to the prescribed regimen. Patients may forget to change the patch at the appropriate times, leading to suboptimal drug delivery.
- **Skin Permeation Variability**: Factors such as skin thickness, hydration level, and local blood flow can affect the permeation of drugs through the skin, leading to variability in drug absorption between individuals.
- **Drug Stability**: Some drugs may degrade when exposed to the conditions required for transdermal delivery, such as heat or moisture. This can limit the shelf life of transdermal patches.
- **Cost:** Transdermal drug delivery systems can be more expensive to manufacture compared to oral medications, which can affect their accessibility and affordability for patients.

APLICATION OF TDDS :

- **Pain Management**: Transdermal patches are commonly used for the management of chronic pain. Drugs like fentanyl, buprenorphine, and lidocaine can be delivered through the skin to provide sustained pain relief over an extended period.
- **Hormone Replacement Therapy (HRT)**: Transdermal patches are used for hormone replacement therapy, delivering hormones such as estrogen and testosterone to alleviate symptoms associated with hormonal imbalances, such as menopause or andropause.
- **Cardiovascular Disorders**: TDDS can be utilized for the treatment of cardiovascular diseases, such as hypertension and angina. Drugs like nitroglycerin and clonidine can be administered through patches to manage these conditions.
- **Smoking Cessation**: Nicotine patches are widely used as a part of smoking cessation programs. They deliver nicotine through the skin, helping to reduce withdrawal symptoms and cravings associated with quitting smoking.
- **Neurological Disorders**: TDDS can be employed for the treatment of neurological disorders such as Parkinson's disease and Alzheimer's disease. Drugs like selegiline and rivastigmine can be delivered transdermally to manage symptoms and improve patient outcomes.
- **Motion Sickness:** Transdermal scopolamine patches are used to prevent motion sickness during travel by delivering the drug continuously through the skin, providing relief from nausea and vomiting.
- **Hormonal Contraception:** Transdermal contraceptive patches containing hormones such as estrogen and progestin are available for birth control. These patches offer a convenient and effective alternative to oral contraceptives.
- **Dermatological Conditions**: TDDS can be used to deliver drugs for the treatment of dermatological conditions such as psoriasis, eczema, and acne. Topical medications can be incorporated into patches for localized treatment.

- **Alzheimer's Disease**: Rivastigmine, a cholinesterase inhibitor used in the treatment of Alzheimer's disease, is available in a transdermal patch form, offering a convenient and consistent delivery method for the drug.
- **Prevention of Osteoporosis**: Transdermal patches containing medications like estrogen or bisphosphonates can be used for the prevention and treatment of osteoporosis in postmenopausal women.

These are just a few examples of the diverse applications of transdermal drug delivery systems across different medical conditions. Their non-invasive nature, convenience, and ability to provide controlled drug release make them valuable options in patient care.

SKIN ANATOMY :

1**. Epidermis** :- The outermost layer of the skin. - It is composed of several layers of cells, including keratinocytes, melanocytes, Langerhans cells, and Merkel cells. - Provides a protective barrier against environmental factors, pathogens and ultraviolet rays.

2. Dermis :- Located beneath the epidermis and contains blood vessels, nerves, hair follicles, and glands. - Composed of connective tissue rich in collagen and elastin fibers that provide structural support and elasticity to the skin. - Contains sensory receptors for touch, pressure, temperature, and pain.

3. Subcutaneous tissue (subcutaneous tissue):- The deepest layer of skin located beneath the dermis.Consists primarily of adipose tissue (fat) and loose connective tissue. Insulates the body, stores energy, and provides shock absorption and protection to major structures such as muscles and bones.

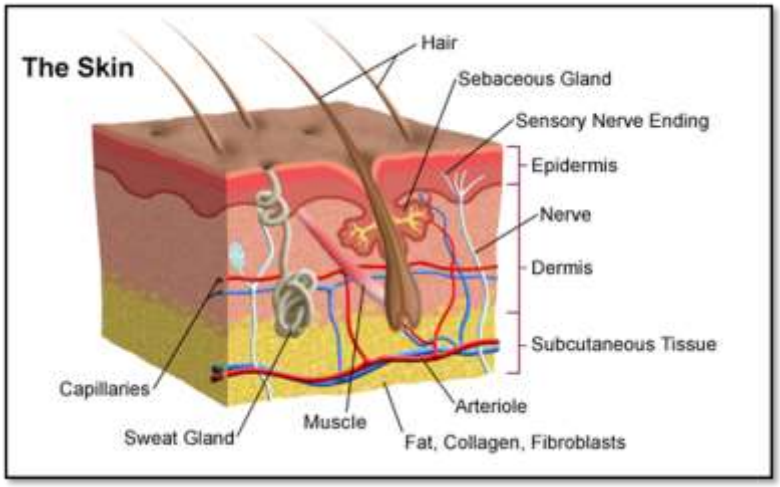

Fig No 1. Anatomy of skin

BASIC COMPONENETS OF TRANSDERMAL DRUG DELIVERY SYSTEMS:

The components of Transdermal device include:

- Polymer
- Drug
- Permeation enhancers
- Other excipients

1. POLYMER

Polymers used in transdermal drug delivery systems (TDDS) serve various functions such as controlling drug release rates, providing adhesion to the skin, and ensuring flexibility of the patch. Some commonly used polymers in TDDS include:

- **Acrylic Polymers:** These are often used as adhesive components in transdermal patches. Examples include polyacrylate and polymethacrylate-based polymers. They provide good adhesion to the skin while allowing for controlled drug release.
- **Silicone Polymers**: Silicone-based polymers offer excellent biocompatibility and flexibility, making them suitable for use in TDDS. They are often used as backing layers or as part of the matrix for drug release.
- **Polyethylene Vinyl Acetate (PEVA)**: PEVA is a copolymer that provides controlled drug release properties. It is commonly used in the matrix of transdermal patches to control the diffusion of drugs through the skin.

- **Polyvinyl Pyrrolidone (PVP):** PVP is a hydrophilic polymer that can enhance the solubility of drugs and improve their penetration through the skin. It is often used in combination with other polymers to optimize drug delivery.
- **Polyethylene Glycol (PEG):** PEG is a water-soluble polymer that can enhance the permeability of drugs through the skin. It is often used as a penetration enhancer in TDDS formulations.
- **Polyurethanes:** Polyurethane-based polymers offer flexibility and mechanical strength, making them suitable for use in TDDS. They are often used as backing layers or as part of the matrix for drug release.

2 DRUG :

In transdermal drug delivery systems (TDDS), the ideal properties of drugs suitable for delivery through the skin include:

- **Appropriate Molecular Weight**: Drugs intended for transdermal delivery typically have molecular weights below 500 Daltons. This size range allows for sufficient permeation through the skin's barrier while maintaining therapeutic efficacy.
- **Optimal Lipophilicity**: Drugs with moderate lipophilicity tend to penetrate the stratum corneum, the outermost layer of the skin, more effectively. However, excessively lipophilic drugs may accumulate in the skin without reaching systemic circulation.
- **Stability**: Drugs intended for transdermal delivery should be chemically stable in the formulation and throughout storage. Stability is crucial to maintaining drug potency and preventing degradation during manufacturing and use.
- **Low Skin Irritation**: Ideally, transdermal drugs should cause minimal irritation or sensitization to the skin to ensure patient comfort and compliance. Irritation can lead to erythema, itching, or other adverse reactions that may limit the utility of the transdermal system.
- **Suitable Solubility**: Drugs must be sufficiently soluble in the formulation matrix to ensure uniform drug distribution and consistent release kinetics. Poor solubility can lead to uneven drug distribution within the patch and erratic drug release.
- **Predictable Pharmacokinetics**: Drugs intended for transdermal delivery should exhibit predictable pharmacokinetic profiles, with consistent absorption rates and plasma concentrations over time. This predictability facilitates dosing regimen optimization and ensures therapeutic efficacy.
- **Therapeutic Window**: The drug's therapeutic window, defined as the range between the minimum effective concentration and the toxic concentration, should allow for safe and effective therapy when delivered via the transdermal route.
- **Sufficient Potency**: Transdermal drugs should have sufficient potency to achieve therapeutic effects at clinically relevant doses. Higher potency allows for smaller patch sizes and reduced frequency of application, enhancing patient convenience and compliance.
- **Non-Toxic Metabolites**: Metabolites generated from drug metabolism should be non-toxic and readily eliminated from the body to minimize the risk of systemic toxicity or adverse effects.
- **Long Duration of Action**: Ideally, transdermal drugs provide sustained therapeutic effects over an extended period, reducing the need for frequent dosing and improving patient adherence to treatment regimens.

3. PENETRATION ENHANCER :

They are substances used to increase the permeability of the skin, facilitating the absorption of drugs into systemic circulation. Common enhancers include lipophilic compounds (e.g., fatty acids, terpenes), hydrophilic agents (e.g., propylene glycol, glycerol), aprotic solvents (e.g., DMSO, DMF), surfactants, cyclodextrins, iontophoresis agents, and physical enhancement techniques (e.g., microneedles, sonophoresis). These enhancers work through various mechanisms, such as disrupting lipid structures, widening intercellular channels, increasing drug solubility, or creating temporary pathways through the skin. Their combined use aims to optimize drug delivery while considering safety and efficacy.

4. OTHER EXCIPIENTS :

These excipients serve different purposes, such as controlling drug release, enhancing stability, providing adhesion to the skin, and improving patient comfort. Here are some common excipients used in TDDS:

- **Polymeric Matrices:** Polymers such as polyethylene vinyl acetate (PEVA), polyvinyl pyrrolidone (PVP), ethylene vinyl acetate (EVA), and acrylic polymers are often used to control drug release rates and provide structural integrity to the patch.
- **Backing Layers:** Materials like polyester, polyethylene, or polyurethane serve as backing layers to protect the patch and provide mechanical support.
- **Adhesive Layers**: Adhesive components such as acrylic adhesives or silicone-based adhesives ensure the patch adheres firmly to the skin while allowing for easy application and removal.
- **Lining Layers:** Lining layers, often made of materials like siliconized release liners or fluoropolymer-coated liners, protect the adhesive layer before application and facilitate patch removal.

- **Plasticizers:** Plasticizers like glycerin or polyethylene glycol (PEG) are added to improve the flexibility and stretchability of the patch, enhancing patient comfort and conformability to the skin.
- **Permeation Enhancers**: As mentioned earlier, permeation enhancers like fatty acids, surfactants, and cyclodextrins are included to increase drug permeation through the skin.
- **Solvents:** Solvents such as ethanol or isopropyl alcohol may be used to dissolve drugs and other excipients, aiding in the formulation process and ensuring uniform drug distribution.

TDDS TYPES :

Transdermal Drug Delivery Systems (TDDS) Can Be Classified Into Several Types Based On Their Mechanism Of Action, Design, And Application Method. Here Are Some Common Types:

1. Matrix Systems: In matrix systems, the drug is dispersed within a polymeric matrix that controls its release. The drug diffuses through the matrix and then permeates through the skin. Matrix systems can provide sustained release of the drug over an extended period.

2. Reservoir Systems: Reservoir systems consist of a drug reservoir sandwiched between a backing layer and an adhesive layer. The drug reservoir contains a saturated solution or suspension of the drug in a liquid or gel vehicle. A membrane controls the release of the drug from the reservoir into the skin.

3. Drug-in-Adhesive Systems: In drug-in-adhesive systems, the drug is dissolved or dispersed within the adhesive layer of the patch. The adhesive layer adheres to the skin, and the drug diffuses from the adhesive layer into the skin over time.

4. Micro-reservoir Systems: These systems utilize micro- or nanostructured technologies to enhance drug delivery through the skin. Examples include microneedle patches, which contain arrays of micron-sized needles that penetrate the stratum corneum to deliver drugs into the underlying skin layers.

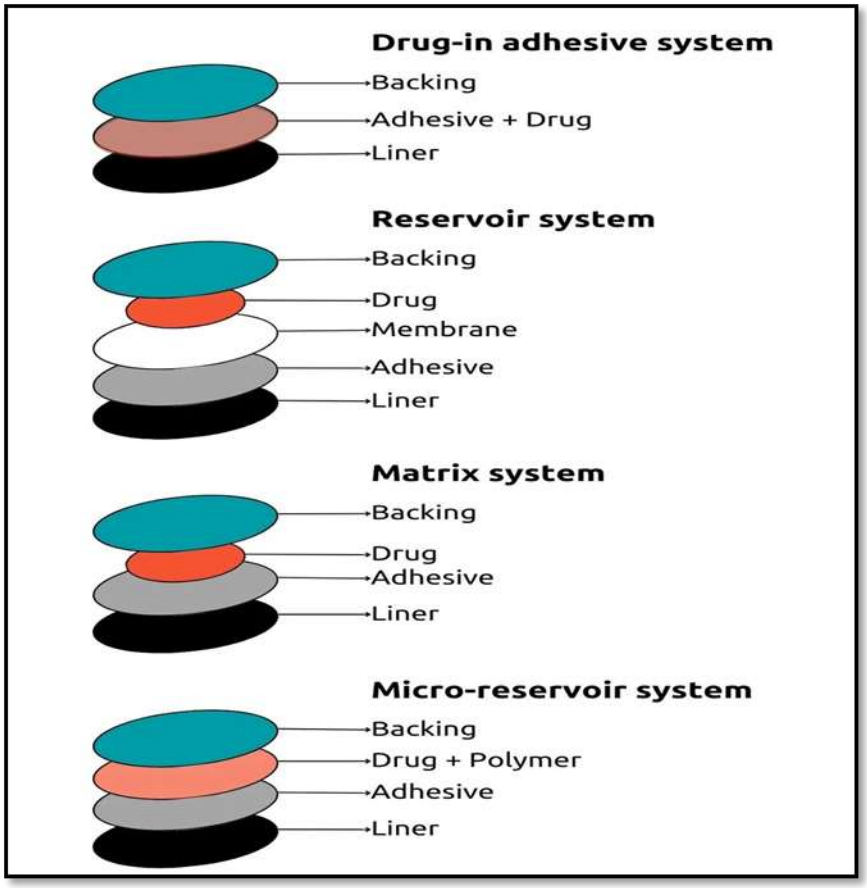

Fig No 2: TYPES OF TDDS

FACTORS AFFECTING TDDS:

Transdermal drug delivery systems are affected by various factors, which can influence the efficacy, safety, and overall performance of the delivery method. Here are some key factors:

- **Skin Permeability**: The skin acts as a barrier to drug absorption. Factors such as skin thickness, hydration level, lipid content, and integrity of the skin barrier influence drug permeation.
- **Drug Properties**: The physicochemical properties of the drug, such as molecular weight, lipophilicity, solubility, and ionization state, impact its ability to penetrate the skin barrier and reach systemic circulation.
- **Formulation Design**: The formulation design, including the type and concentration of penetration enhancers, solvents, and additives, affects drug permeation and skin compatibility.
- **Patch Design**: The design of the transdermal patch, including the composition of the backing, adhesive, membrane, and drug reservoir, influences drug release kinetics, stability, and adhesion to the skin.
- **Application Site**: The site of application on the body can affect drug absorption due to variations in skin thickness, blood flow, and permeability.
- **Skin Conditions**: Skin conditions such as inflammation, burns, abrasions, and diseases can alter skin permeability and affect drug absorption.
- **Temperature and Moisture**: Environmental factors such as temperature and humidity can influence skin permeation by affecting skin hydration and the mobility of drug molecules within the skin layers.
- **Physical Activity and Movement**: Physical activity and movement can affect drug absorption by altering skin microcirculation and the contact between the patch and the skin.
- **Individual Variability**: Variations in individual factors such as age, gender, ethnicity, genetics, and skin physiology can impact the efficacy and variability of transdermal drug delivery.
- **Regulatory Considerations**: Regulatory requirements and guidelines for transdermal drug delivery systems, including safety, efficacy, and quality standards, influence product development and approval processes.

Understanding and optimizing these factors are crucial for the successful design and development of transdermal drug delivery systems to ensure effective and safe drug delivery.

CONCLUSION :

The transdermal drug delivery systems (TDDS) highlights its pivotal role in modern pharmaceutical advancements. Offering a non-invasive and patient-friendly approach, TDDS presents a significant improvement over traditional drug administration methods. By ensuring controlled and sustained release of medications, it maintains stable plasma levels over time, reducing the likelihood of dosage-related fluctuations and enhancing therapeutic efficacy. Moreover, TDDS minimizes gastrointestinal side effects and hepatic degradation, thereby improving drug tolerability and safety profiles. This technology not only enhances the bioavailability of drugs with poor oral absorption but also accommodates a wide range of therapeutic agents, including small molecules, peptides, and large biologics. Its flexibility and versatility not only improve patient compliance but also open doors for tailored therapy approaches, potentially revolutionizing personalized medicine. Ultimately, the advantages of TDDS encompass convenience, comfort, and effectiveness, promising to significantly impact patient care across diverse medical domains.

REFERENCE :

1. Roge Ashish B, Sakhare Ram S, Bakal RL, Channawar MA, Bakde BV, Gawande SR , Chandewar AV. Ethosomes: Novel Approach in Transdermal Drug Delivery System. Research J. Pharma. Dosage Forms and Tech. 2010; 2(1): 23-27.
2. Hanumanaik M, Patil U, Kumar G, Patel S K, Singh I, Jadatkar K. Design, Evaluation and Recent Trends in Transdermal Drug Delivery System: A Review. International Journal of Pharmaceutical Sciences and Research. 2012; 3(8): 2393-2406.
3. T. Venkateswara Rao, Owku Ravi Kiran. Review: Transdermal patch. Research J. Pharma. Dosage Forms and Tech. 2013; 5(1): 12-16.
4. Chandrashekhar N S, Shobha Rani R H. Physicochemical and Pharmacokinetic Parameters in Drug Selection and Loading of Transdermal Drug Delivery. Indian Journal of Pharmaceutical Sciences. 2008; 70(1): 94-96.
5. Y. Krishna Reddy, D. Maheswara Reddy, V. Saroja, S.K. Maimoon. Transdermal Drug Delivery System: A Review. Research J. Pharma. Dosage Forms and Tech. 2013; 5(4): 202-12.
6. Ghosh, T.K. and Banga, A.K. Methods of enhancement of transdermal drug delivery: Part I. Physical and Biochemical Approaches. Pharmaceutical Technology.1993; 75-78.6. Chein YW. Transdermal Controlled Systemic Medication. New York and Basel: Marcel Dekker Inc; 1987.

7. Patel D, Chaudhary SA, Parmar B, Bhura N. Transdermal drug delivery system: a review. Pharm Innov. 2012; 1: 66–75.
8. Bowen, A.J., John, V.A., Ramirez, M.E. and Good, W.R. Bioavailability of oestradiol from the Alora (0.1 mg/day) oestradiol matrix transdermal delivery system compared with Estraderm (0.1 mg/day), J. Obstet and Gynecol. 1998; 18(6): 575-580.
9. Davila, G.W., Daugherty, C.A. and Sanders, S.W. A short term multicenter, randomized, double-blind dose titration study of the efficacy and anticholinergic side effects of transdermal compared to immediate release oral oxybutynin treatment of patients with urge urinary incontinence, J. Urol 2001; 166: 140-145.
10. Patel D, Chaudhary SA, Parmar B, Bhura N. Transdermal drug delivery system: a review. The Pharm Innovation. 2012;1(4):66-75.
11. Dhiman S, Thakur GS, Rehni AK. Transdermal patches: a recent approach to new drug delivery system. Int. J Pharmacy Pharm Sci. 2011;3(5):26-34.
12. Scheindlin S. Transdermal Drug Delivery: Past, Present, Future. Molecular Interventions. 2004; 4(6): 308-312.
13. Darwhekar G, Jain Dk, Paditar Vk. Formulation and Evaluation of Transdermal Drug Delivery System of Clopidogrel Bisulfate. Asi. J. Pharmacy Life Sci. 2011; 1(3): 269-278.
14. Berner B, John Va. Pharmacokinetic Characterization of Transdermal Delivery System. J. Clin. Pharmaco. 1994; 26(2): 121-134
15. Arunachalam A, Karthikeyan M, Kumar Vd, Prathap M, Sethuraman S, Ashutoshkumar S, Manidipa S. Transdermal Drug Delivery System: A Review. Current Pharma Res. 2010; 1(1):70-81.
16. Kumar Sr, Jain A, Nayak S. Development and Evaluation of Transdermal Patches of Colchicine. Der Pharmacia Lettre. 2012; 4(1): 330-343.
17. Patel, D., Sunita, A., Parmar B., Bhura N., Transdermal Drug Delivery System: A Review. The Pharma Innovation. 2012; 1(4): 66-75.
18. Sharma N., Agarwal G., Rana A.C., Ali Bha Tz.,Kumar D. A Review: Transdermal Drug Delivery System: A Tool for Novel Drug Delivery System. International Journal of Drug Development & Research. 2011; 3(3): 70-84. [41] Das, U. S., Pande K.H., an Overview of Diabetes Mellitus, World Journal of Pharmacy and Pharmaceutical Sciences. 2013; 2(1): 161-178