## Review of Literature Contents

<table>
<thead>
<tr>
<th>SR NO</th>
<th>TOPIC</th>
<th>PAGE NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Review of Work Done on Transdermal Drug Delivery System.</td>
<td>31</td>
</tr>
<tr>
<td>2</td>
<td>Review of Work Done on Transdermal Patch of Antihypertensive Drugs.</td>
<td>34</td>
</tr>
<tr>
<td>3</td>
<td>Review of Work Done on Different Transdermal Film Forming Agents &amp; Permeation Enhancers</td>
<td>35</td>
</tr>
<tr>
<td>4</td>
<td>Review of Work Done on Animal Skin, Human Cadaver Skin And Animal Models</td>
<td>37</td>
</tr>
</tbody>
</table>
2.1 REVIEW OF WORK DONE ON TRANSERMAL DERMAL DRUG DELIVERY SYSTEM

Madhura SD et al had discussed that the transdermal drug delivery exhibits two main advantages over the conventional oral delivery, by-passing the hepatic first-pass, and maintaining the plasma drug level at a plateau over a long period of time. Thus the drug transfer through the skin reaches a constant rate under stationary conditions after a short time under transient conditions. The monolithic device can maintain a constant drug delivery only when the diffusivity of the drug through this polymer is very high. In association with a reservoir, this device becomes more efficient. The system made of a porous polymer with convective transfer of the drug appears to be more effective, providing a constant drug concentration on the skin surface, which is responsible for a constant rate of drug transfer through the skin and a constant plasma drug level over a long period of time[51].

Narayanacharyulu R et al had explained that transdermal flux of felodipine across the skin improved by the use of organic solvent and penetration enhancer. In their study they designed model to study the effect of ethanol as a permeation enhancer in matrix and reservoir system[52].

Patel NB et al had designed new method for dissolution study of transdermal device. This method required one convex screen patch holder, which fixed at the bottom of a dissolution vessel in such a way between the apex of a convex screen and the bottom of a dissolution vessel for holding the device. The dissolution of nitroglycerin (GTN) of marketed products, with two different sizes, performed with new method and compared with existing method. The results suggested that this new method was reproducible and applicable for in vitro characterization of marketed transdermal devices[53].

Darwhekar G et al had prepared transdermal patches of Clopidogrel Bisulfate and described that if sufficient water can flow through the membrane to alter the hydration state of the hydrophilic matrix, diffusional parameters in the delivery system may also be affected. This may be a particular problem for occlusive patches applied to the skin over extended periods of time. In their
study they explained mathematical solution which provides best correlation between experimental results and calculated results\textsuperscript{[54]}.

**Patel KD et al** had prepared and evaluated transdermal adhesive patches of timolol maleate using hydrophilic and lipophilic polymers. They suggested that permeation of drug through the different layers of skin improve with combination of propylene glycol and myristic acid was higher than the alone use of them\textsuperscript{[55]}.

**Thacharodi D et al** Prepared matrix type of nifidipine by solvent casting technique. Six formulations were composed by using sodium alginate, different polymeric grades of HPMC and different plasticizers like PEG-400 and PG. The prepared matrix patches were evaluated for physicochemical parameters, *in-vitro* drug release and permeation study. By fitting the data, it was concluded that drug release from matrix films followed zero order release model and the data confirm the feasibility of developing TDDS of nifidipine for potential therapeutic use\textsuperscript{[56]}.

**Jain S et al** studied investigate for increase bioavailability of transdermal patch of Captopril. The matrix type patches were prepared by using solvent evaporation method for the study of, effect of polymer composition, plasticizer and permeation enhancer on the physico-mechanical, *in-vitro* drug release characteristics and *ex vivo* skin permeation of the film. The physico-mechanical parameters gives better results and also skin irritation studies showed no irritancy\textsuperscript{[57]}.

**Gavali P et al** formulate matrix-type transdermal therapeutic system containing drug enalapril maleate by solvent evaporation technique. Different concentrations of isopropyl myristate were used, prepare and evaluate. The results indicate that the formulation containing highest amount of isopropyl myristate gives better penetration of enalapril maleate through goat skin\textsuperscript{[58]}.

**Namara V et al** develop and evaluate transdermal therapeutic system of drug carvedilol with different concentration of drug and hydrophobic (ethyl cellulose) polymeric system by the solvent evaporation technique by using di-butyl phthalate to the polymer weight incorporated as plasticizer. Obtained
results of physicochemical parameters and drug release study suggested good permeation of carvedilol from transdermal matrix patches.\[59\].

**Kanikkannan N et al** investigated transdermal patch of prochlorperazine maleate for avoid nausea and vomiting acutely and over a prolonged period of time during pregnancy occurs side effect from *Hyperemesis gravidarum*. Prochlorperazine maleate is the drug of choice for the treatment with long dosage regimen so avoid these side effects modulating it in to transdermal patch. It was found that the film made of 0.05% PVA was found to be the most effective due to the physicochemical studies as performed and irritation tests. The formulated film is expected to give the maximum patient compliance, avoiding first pass hepatic metabolism.\[60\].

**Ramesh G et al**, prepared and evaluated transdermal matrix patches of Nitrendipine by the solvent evaporation technique. The obtained results revealed that Nitrendipine release from the matrix patch in a continuous manner for a predetermined time from the polymeric matrix of Eudragit RL 100 and HPMC K 15M.\[61\].

**Barry B W et al**, prepared transdermal matrix patch of ketoprofen, evaluated for its permeation profile and pharmacological effects, and obtained results compared with the results of oral administration. Obtained results revealed that transdermal device of ketoprofen avoid side effects of oral delivery.\[62\].

**Murthy S.N. et al** had developed transdermal formulation containing Theophylline and Salbutamolsulfate in a combination. The formulations were subject to *in vitro* diffusion release studies and result suggested controlled release of drug from the transdermal matrix up to predetermined period.\[63\].
2.2 REVIEW OF WORK DONE ON TRANSMERAL PATCH OF ANTIHYPERTENSIVE DRUGS

Dorle AK et al prepared diltiazem Hydrochloride loaded transdermal patch by solvent evaporation method. The prepared patches examine for physicochemical and release study. Obtained results revealed that from the prepared patches drug release in a continuous manner for a long period and it overcome problems associated with oral drug delivery\[64\].

Mohammad R et al prepared matrix patches of Carvedilol and evaluated for weight uniformity, hardness, friability, drug content uniformity and in vitro drug release characteristics. Obtained results suggested that all the fabricated tablets delivered the drug follow higuchi diffusion mechanism and the drug release follow Fickian transport mechanism\[65\].

Gunjan S et al developed once daily matrix patches of water soluble drug diltiazem hydrochloride using natural polymers and gums. patches were prepared by solvent evaporation method. Taro mucilage gum sustained the drug release effectively for 24 hrs. The results have shown that formulations followed first order kinetics and the patches can be useful as once daily formulation\[66\].

Ahad H et al developed matrix transdermal systems of Diltiazem HCl using various proportions of Ficusglomeratafruit mucilage by using solvent evaporation method. The experimental results shows that the release of drug from the patch delayed in controlled manner as the proportion of Ficusglomerataincreased and Diltiazem HCl could be develop as transdermal patches with Ficusglomeratafruit mucilage\[67\].
2.3 REVIEW OF WORK DONE ON DIFFERENT TRANSDERMAL FILM FORMING POLYMERS & PERMEATION ENHANCERS

Hanan M et al prepared and evaluated transdermal matrix patch of timolol maleate to study the effect combination of polymers and polymeric matrix on drug release from the patch across the skin. They tried Eudragit RL 100 and RS 100 combination for the preparation of transdermal matrix patch. Obtained results of drug release study suggested that from the polymeric matrix drug was continuously release for a predetermined period.[68]

Jain S et al had prepared matrix patch of captopril. Prepared patches were evaluate for physicochemical parameters and in vitro drug release through the wistar rat skin. Obtained results revealed that patches had sufficient mechanical strength and drug release in a continuous manner for a long period from the polymeric matrix. It also suggested that transdermal delivery of captopril improve its efficacy and overcome the problems associated with oral delivery.[69]

Pachisia N et al has prepared transdermal matrix patch of pinacidil using Eudragit RL 100 and PVA. Patches were evaluated for various physicochemical parameters and drug permeation study. Obtained results suggested that polymeric matrix of hydrophilic and lipophilic polymer play a major role on drug permeation through the skin.[70]

Jadhav j et al had prepared matrix type transdermal patches of indomethacin using different ratio of ethyl cellulose / polyvinyl pyrrolidone (PVP) and Eudragit RL-100 / Eudragit RS 100 by solvent evaporation technique. Prepared batches were subjected to physiochemical studies and in vitro drug release study. The results suggest that patches had sufficient mechanical drug release property. Based on obtained results, transdermal matrix patches prepared with optimum ratio of Eudragit RL 100 and RS 100 were selected as an optimized one. Optimized batch subjected for in vivo experiment and skin irritation test.[71]

Agrawal SS et al had prepared adhesive patches of metoprolol tartrate using mercury casting method. Prepared patches were evaluated for
physicochemical parameters and drug release study. The results revealed that patches have sufficient mechanical strength along with continuous drug release\(^{[72]}\).

**Rao M et al** had developed transdermal device of nitredipine using Eudragit RL 100 and PVP. Drug permeation studies results indicate that drug release from the matrix device depend on thickness of polymeric matrix and concentration of polymers\(^{[73]}\).

**Ghosh B et al** had prepared transdermal multi adhesive type patches of nicorandil using various acrylic polymers. The results of *in vitro* study shows that drug continuously and in a controlled manner release from the prepared patches of combination of Eudragit RL and RS\(^{[74]}\).

**Guyot M et al** had fabricated matrix transdermal patch contain propranolol using different polymer i.e. RS 100 and RL 100 of Eudragit, Ethyl cellulose and PVP. *In-vivo* isolated skin permeation study through human cadaver skin was conducted to determine the availability of propranolol from the TDDS. The permeation through the skin follows the first order kinetics\(^{[75]}\).

**Paochu W et al** had prepared adhesive matrix transdermal patches containing Nicardipine hydrochloride, oleic acid as the skin penetration enhancer, Eudragit RL100, triacetin and citric acid and evaluated them in terms of their uniformity, skin irritation and *in vivo* skin permeation\(^{[76]}\).
2.4 REVIEW OF WORK DONE ON ANIMAL SKIN, HUMAN CADAVER SKIN & ANIMAL MODEL

Vijayan V et al has prepared nicotine transdermal matrix patches to overcome problems of tobacco. Prepared patches evaluated for in - vitro permeation study using cobra skin. Cobra skin collects from the head, body and tail portion. Flux was calculated with this different skin site to find out effect on drug release. Fluxes of nicotine through cobra skin (CS) taken from the head, body, and tail were 233.93±16.08, 206.87±19.00, and 211.26 ± 22.93 mg/cm²/hr¹/², respectively (n=6). These results revealed that there was no significant difference in drug release from the cobra skin collect at different site[77].

Darwhekar G et al performs drug permeation study of prepared patches using franz diffusion cell in which they use human cadaver skin as a membrane. In this study, they found that stratum corneum had significant effect on drug release from the patch. Study performs after removing stratum corneum shows higher skin flux than with stratumcornium. They also suggested that hydrated epidermis along with heat also improve drug permeation through the skin [78].

Mohammad R et al had prepared and evaluated patches to study the effect of permeation enhancer and type of skin membrane on drug release through the polymeric matrix of prepared patches. They performed in vitro release study on rat skin, hairless mouse skin, hairless guinea pig skin, and human cadaver skin using the contraceptive drug Levonorgestrel. The results suggested that from the hairless mouse skin shows highest release and human cadaver skin shows lowest drug release[79].

Barry B.W. et al stated that when human skin is available, the biological diversity in its permeability between species and within samples from one specimen or individual poses a problem. Even with close control of laboratory conditions and experimental technique, the variability for replicate experiments may exceed that for a well-designed in vivo procedure[80].