SUMMARY AND CONCLUSION
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The aim of current study was to formulate and optimize the transdermal patches of Verapamil hydrochloride (VPML), Trandolapril (TPL) and Perindopril (PPL) and to develop the efficiency, reduce the frequency of dosage, for extensive release of the drugs and better patient compliance.

Preformulation study of the drugs was carried primarily, to distinguish the physicochemical parameters such as partition coefficient, melting point, compatibility and solubility studies as per standard methods. Drug loaded transdermal patches were prepared by solvent casting method by means of various polymers such as polycarbophil, hydroxy propyl methyl cellulose, chitosan, sodium carboxymethylcellulose, polyvinyl alcohol, polyvinyl pyrrolidone K30, carbopol 934P, eudragit RL 100 and sodium alginate.

Prepared patches were estimated for weight variation, drug content, folding endurance test, loss of moisture, moisture uptake, thickness in vitro release and in vitro permeation.

The results of preformulation studies specifies that the chosen drugs were ideal candidates for transdermal delivery and were compatible with the polymers employed in the study which was established by DSC and FTIR studies.
**Perindopril (PPL) transdermal patches**

PPL transdermal films were prepared by solvent casting method by means of eudragit RL 100, hydroxypropylmethylcellulose, carbopol 934P and sodium carboxymethylcellulose as polymers. DMSO and Propylene glycol were used as penetration enhancer and plasticizer correspondingly. Dichloromethane, methanol and ethanol were utilized as solvents.

The drug content in all the patches was found to be identical. The patches were weighing in between 26.09 mg to 27.28 mg. Patch thickness was in the range of 253 µm to 291 µm. Folding endurance studies exhibited that the formulation PPL 4 exhibited maximum value followed by PPL 1, PPL 2 and PPL 3 correspondingly and illustrated significant variation.

*In vitro* release studies evidently illustrated that the percent release of PPL was found to be highest for PPL 2 (91.42±1.74%). The order of drug release was found to be PPL 2>PPL 4>PPL 1>PPL 3.

*In vitro* permeation study of formulation PPL 2 exhibited highest release of drug (90.63±6.21%) in 24 hr, the order of drug release is PPL 2>PPL 4>PPL 1>PPL 3. All formulations followed Korsmeyer – Peppas release kinetics with non-Fickian diffusion mechanism.

The mean steady state flux ($J_{ss}$) was found to be 0.1338±0.01, 0.2273±0.01, 0.1156±0.009 and 0.148±0.01 mg/cm²/hr and the permeability coefficient was found to be 0.0335±0.003, 0.057±0.002, 0.0289±0.002 and 0.04±0.003 cm/hr for the formulations PPL 1, PPL 2, PPL 3 and PPL 4 correspondingly.
The results of the stability studies revealed that there was significant alteration in drug content. The records of in vitro permeation was scrutinized by t test and significant variation was noted between means at 5-8 and 12 hours. The cumulative percentage of PPL permeated in 24 h was found to be 84.93±3.56%. Permeability coefficient and flux of PPL 2 was found to be 0.1481±0.05 mg/cm²/hr and 0.0370±0.01 cm/hr correspondingly.

In vitro permeation profile of PPL 2 after stability study could be best articulated by Korsmeyer-Peppas model, as the plots exhibited maximum linearity (r²:0.9298) and the attained release exponent (n) value, 0.9942, supported non Fickian release.

**Trandolapril (TPL) transdermal patches**

TPL transdermal films were prepared by solvent casting method by means of hydroxypropylmethylcellulose, chitosan, povidone polyvinyl alcohol and carbopol 934P as polymers. DMSO and Propylene glycol were used as penetration enhancer and plasticizer correspondingly. Methanol, Acetic acid, dichloromethane and ethanol were utilized as solvents.

The drug content in all the patches was found to be identical. The patches were weighing in between 26.79 mg to 29.12 mg. Patch thickness was in the range of 251 µm to 274 µm. Folding endurance studies exhibited that the formulation TPL 3 illustrated highest value followed by TPL 2, TPL 4 and TPL 1 respectively and showed considerable variation.
In vitro release studies clearly exhibited that the percent release of TPL was found to be highest for TPL 2 (87.46%). The order of drug release was found to be TPL 2>TPL 3>TPL 1>TPL 4.

In vitro permeation study formulation TPL 2 exhibited highest release drug (84.21%) in 24 hrs, this formulation was considered as optimized one and employed for more study. The order of drug release is TPL 2>TPL 3>TPL 1>TPL 4. All formulations followed Korsmeyer – Peppas release kinetics, with non-Fickian diffusion mechanism.

The mean steady state flux ($J_{ss}$) was found to be 0.1411±0.012, 0.1527±0.011, 0.1464±0.008, 0.1349±0.01 mg/cm²/hr and the permeability coefficient was found to be 0.0353±0.003, 0.0381±0.003, 0.0366±0.002, 0.0337±0.003 cm/hr for the formulations TPL 1, TPL 2, TPL 3 and TPL 4 correspondingly.

The results of the stability studies exposed that there was considerable alteration in drug content. The record of in vitro permeation was examined by t test and there was no considerable variation between means. The cumulative percentage of TPL 2 permeated in 24 h was found to be 79.86±3.15%. Flux and permeability coefficient of TPL was found to be 0.1463±0.01 mg/cm²/hr and 0.0365±0.002 cm/hr correspondingly.

In vitro permeation profile of TPL 2 after stability study could be best articulated by Korsmeyer – Peppas model, as the plots exhibited maximum linearity ($r^2$:0.9461) and the attained release exponent (n) value, 0.998, supported non Fickian release.
Verapamil hydrochloride (VPML) transdermal patches

VPML transdermal patches were prepared by solvent casting method by means of sodium carboxymethylcellulose, hydroxypropylmethylcellulose, polycarbophil and sodium alginate as polymers. DMSO and Glycerine were utilized as penetration enhancer and plasticizer correspondingly. Methanol, dichloromethane and Ethanol were utilized as solvents.

The drug content in all the patches was found to be identical. The patches were weighing in between 26.22 mg to 28.28 mg. Patch thickness was in the range of 246 µm to 281 µm. Folding endurance studies showed that the formulation VPML 3 illustrated highest value followed by VPML 2, VPML 4 and VPML 1 correspondingly and demonstrated considerable variation.

CONCLUSION

Perindopril (PPL)

In vitro release studies evidently illustrated that the percent release of PPL was found to be highest for PPL 2 (91.42±1.74%). The order of drug release was found to be PPL 2>PPL 4>PPL 1>PPL 3.

In vitro permeation study of formulation PPL 2 illustrated maximum release of drug (90.63±6.21%) in 24 hr, and this formulation was measured as optimized one and used for more study. The order of drug release is PPL 2>PPL 4>PPL 1>PPL 3. All
formulations followed Korsmeyer – Peppas release kinetics with non-Fickian diffusion mechanism.

The mean steady state flux ($J_{ss}$) was found to be $0.1338 \pm 0.01$, $0.2273 \pm 0.01$, $0.1156 \pm 0.009$ and $0.148 \pm 0.01$ mg/cm$^2$/hr and the permeability coefficient was found to be $0.0335 \pm 0.003$, $0.057 \pm 0.002$, $0.0289 \pm 0.002$ and $0.04 \pm 0.003$ cm/hr for the formulations PPL 1, PPL 2, PPL 3 and PPL 4 correspondingly.

The results of the stability studies exposed that there was considerable alteration in drug content. The records of in vitro permeation were scrutinized by $t$ test and considerable variation was observed between means at 5-8 and 12 hours.

The cumulative percentage of PPL permeated in 24 h was found to be $84.93 \pm 3.56\%$. Flux and permeability coefficient of PPL was found to be $0.1481 \pm 0.05$ mg/cm$^2$/hr and $0.0370 \pm 0.01$ cm/hr correspondingly.

In vitro permeation profile of PPL 2 after stability study could be best articulated by Korsmeyer-Peppas model, as the plots illustrated maximum linearity ($r^2:0.9298$) and the acquired release exponent (n) value, 0.9942, supported non Fickian release.

**Trandolapril (TPL)**

In vitro release studies clearly illustrated that the percent release of TPL was found to be highest for TPL 2 (87.46%). The order of drug release was found to be TPL 2>TPL 3>TPL 1>TPL 4.
In vitro permeation study formulation TPL 2 exhibited highest release drug (84.21%) in 24 hrs, this formulation was considered as optimized one and used for more study. The order of drug release is TPL 2>TPL 3>TPL 1>TPL 4. All formulations followed Korsmeyer – Peppas release kinetics with non-Fickian diffusion mechanism.

The mean steady state flux ($J_{ss}$) was found to be 0.1411±0.012, 0.1527±0.011, 0.1464±0.008, 0.1349±0.01 mg/cm²/hr and the permeability coefficient was found to be 0.0353±0.003, 0.0381±0.003, 0.0366±0.002, 0.0337±0.003 cm/hr for the formulations TPL 1, TPL 2, TPL 3 and TPL 4 correspondingly.

The results of the stability studies revealed that there was considerable change in drug content. The records of in vitro permeation was scrutinized by t test and there was no significant variation between means.

The cumulative percentage of TPL permeated in 24 h was found to be 79.86±3.15%. Permeability coefficient and flux of TPL was found to be 0.1463±0.01 mg/cm²/hr and 0.0365±0.002 cm/hr correspondingly.

In vitro permeation profile of TPL 2 after stability study could be best articulated by Korsmeyer – Peppas model, as the plots exhibited maximum linearity ($r^2$:0.9461) and the attained release exponent ($n$) value, 0.998, supported non Fickian release.

Patches were developed to a suitable level in terms of their physicochemical parameters. Further these formulations were found
to have an extensive release of the drug upto a period of 24 hours during *in vitro* permeation studies.

The current study established the prospect of scheming a buccal drug delivery system for Trandolapril may be more efficient than the conventional oral delivery and could be a superior option of drug delivery system in the management of hypertension.

**VERAPAMIL (VPML)**

*In vitro* release studies clearly exhibited that the percent release of VPML was found to be highest for VPML 1 (94.24±0.94%). The order of drug release was found to be VPML 1>VPML 2>VPML 3>VPML 4.

*In vitro* permeation study of formulation VPML 1 exhibited maximum release of drug (93.24±5.1%) in 24 hrs, and this formulation was considered as optimized one and used for more study. The order of drug release found to be VPML 1>VPML 2>VPML 3> VPML 4. All formulations followed Korsmeyer – Peppas release kinetics with non- Fickian diffusion mechanism.

The mean steady state flux (J_{ss}) was found to be 0.4152±0.03, 0.3863±0.017, 0.3836±0.01, 0.3495±0.002 mg/cm²/hr and the permeability coefficient was found to be 0.4152±0.003, 0.0386±0.001, 0.0383±0.001, 0.0349±0.00 cm/hr for the formulations VPML 1, VPML 2, VPML 3 and VPML 4 correspondingly.

The results of the stability studies exposed that there was considerable alteration in drug content. The records of *in vitro* permeation was scrutinized by *t* test and considerable variation was
noted between means at 1, 3 and 6-9 hours. The cumulative percentage of VPML 1 permeated in 24 h was found to be 88.25±3.52%. Flux and permeability coefficient of VPML was found to be 0.3962±0.09 mg/cm²/hr and 0.0392±0.009 cm/hr correspondingly.

In vitro permeation profile of VPML 1 after stability study could be best articulated by Korsmeyer-Peppas model, as the plots demonstrated maximum linearity (r²:0.947) and the attained release exponent (n) value, 0.9968, supported non Fickian release.

Patches were developed to a satisfactory level in terms of their physicochemical properties, bioadhesive strength, in vitro release and ex vivo permeation. Further these formulations were found to have an extended release of the drug during in vitro permeation studies. The present study demonstrated the possibility of designing a transdermal delivery system for these antihypertensive drugs which will be more bioavailable, efficacious than the conventional delivery and so could be a better drug delivery system of choice in treatment of hypertension. So the optimized formulations may further be subjected to long term stability studies as per ICH guidelines, study in healthy human volunteers to establish pharmacokinetic safety and scaling up for further commercial exploitation.