ISSN No:-2456-2165

# Studies on Formulation and Evaluation of Buccal Patch for Delivery of an Anti-Hypertensive Drug

Mahesh Mane*, Nilesh Patole*, Tejaswini Jadhav
Mandesh Institute of Pharmaceutical Science and Research Center Mhaswad

**Abstract:- In that study includes prepared and evaluate the buccal patches of Losartan potassium used various polymers such as an ethyl cellulose, Hydroxypropyl methylcellulose Eudragit 100 in different concentration and combination, like polyvnylalchohol used as plasticizer and Dimethyl sulfoxide used as penetration enhancers. All batches were formulated by solvent casting technique. Losartan potassium an antihypertensive drug has high first pass metabolism so buccal route is superlative for its systemic delivery there by produce excellent bioavailability. Preformulation study performed and patches prepared were assessed for evaluation of different physicochemical parameters like uniformity of weight, thickness, content uniformity and folding endurance. In vitro studies shows that release rate of Losartan potassium was higher from films containing ratio of Eudragit L 100 and Ethyl cellulose in proportion of 2:1 ratio and drug release after 5hrs.Was found to be 95.13%.**

**Keywords:-** buccal patch, Losartan Potassium, penetration enhancers, solvent casting technique.

## I. INTRODUCTION

Throughout the various routes of drug delivery, oral route is excellent the most preferred to the patient and the psychologist. After all, administration of drugs has disadvantages such as hepatic first metabolism and enzymatic degradation within the GI tract, that prevent oral administration of certain classes of drugs specially peptides and proteins.[1]Mucoadhesive drug delivery systems are delivery systems, which utilized the property of bio adhesion of various polymers, which become adhesive on hydration and therefore can be used for targeting a drug to appropriate region of the body for lengthy period of time. The basic content of buccal drug delivery system are drug substance, bio adhesive polymers, backing membrane, permeation enhancers.[2]The traditional type of buccal dosage forms are buccal tablets, troches, mouth washers, lozenges and bucal patch. Buccal film may be favored over adhesive tablet in terms of flexibility and comfort. In addition, they can overcome the relatively short residence time of oral gels on the mucosa, which is easily washed away and evacuated by saliva.[3]Moreover; the buccal film is able to protect the wound surface, thus reduce pain and also could treat oral diseases more effectively. The concept of bio adhesion is commonly used to describe the adhesion between polymer either synthetic or natural to soft tissue. In instances when bond is generate between mucus membrane and polymer, at that time term of mucoadhesion is used. Mucus membrane is one, which is goblet cells are present for the secretion of mucus, which is composed of glycoprotein mucin.[4]Buccal patch is a non- dissolving thin matrix modified release dosage form combination of one or more polymer films or layers containing the drug and/or other excipients the patch may contain a mucoadhesive polymer layer which bonds to the oral mucosa, oral cavity. The patch is detached from the mouth and disposed of after a particular time.[5]Buccal drug delivery is a auspicious area for continued research with the destination of systemic delivery of orally inefficient drugs as well as attractive and attainable for non-invasive delivery of potent peptide and protein drug molecules Losartan potassium are class of antihypertensive drugs that are used to treat hypertension. Amid the very important and mostly used drugs are thiazide diuretics, calcium channel blockers, ACE inhibitors, angiotensin II receptor antagonists and beta blockers. Losartan, and angiotensin II receptor antagonist is used to control of high blood pressure. The purpose of present investigation was to prepare mucoadhesive buccal patches of Losartan to ensure satisfying drug release in mouth cavity with the use of blends of hydrophilic and hydrophobic polymers and thereby to escape first pass metabolism and longtime duration of action and consolidation of the hydrophilic and hydrophobic polymers on in-vitro release profiles of patches prepared by solvent casting method was regulate.

ISSN No:-2456-2165

## II. MATERIAL AND METHODS

Losartan potassium, Hydroxypropyl methyl cellulose, Ethyl cellulose, Eudragit L 100, Aspartame, Ethanol, polyvinyl alcohol (PVA), Dichloromethane were received as gift sample from research laboratory, Mumbai India.

| Back | F1 | F2 | F3 | F4 | F5 |
|---|---|---|---|---|---|
| Losartan Potassium(mg) | 25 | 25 | 25 | 25 | 25 |
| HPMC(mg) | 100 | 150 | 200 | - | 150 |
| Ethyl Cellulose (mg) | 200 | 150 | - | 100 | 50 |
| Eudragit L-100(mg) | __- | - | 100 | 200 | 100 |
| Dimethyl Sulphoxide (ml) | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 |
| PVA (%) | 2% | 2% | 2% | 2% | 2% |
| Dichloromethane(ml) | 5 | 5 | 5 | 5 | 5 |
| Ethanol(ml) | 5 | 5 | 5 | 5 | 5 |
| Aspartame (mg) | 2 | 2 | 2 | 2 | 2 |

Table 1: formulation of buccal patch Losartan Potassium using different concentration of polymer

*A. Pre-formulations studies:*

a) Calibration curve of Losartan potassium
Stock solution ofLosartan potassium 100 µg/ml of was prepared in solvent phosphate buffer (pH 6.8) and further afterwards diluted with phosphate buffer to achievethe solutions with concentration range 1-5µg/ml. Then solution filtered and analyzed spectrophotometrically at 227 nm using UV-Spectrophotometer (Jasso V630, Japan) and standard curve was plotted and calculated the values of slope, intercept and coefficient of correlation.

b) Compatibility studies between drug and excipients:
Incompatibility is the conclude of mixing of two or more substances and is identified by physical, chemical and therapeutic qualities. It may affect the safety, efficacy and appearance of the dosage form. It is hence of prime priority for formulation to determine between active ingredient(s) and excipient(s) use to make possible incompatibility final dosage form. In this study, we examined infrared analysis to detect any chemical or physical interaction or drugs and polymer bonds formation.

*B. FTIR Studies:*

Infrared spectroscopy is most capable analytical techniques which offer the possibility of chemical identification. This facility when coupled with intensity measurements may be used for quantitative analysis.Most important advantages of IR over the other usual methods of structural analysis is that it gives useful knowledge about the structure of molecule quickly, without tiresome evaluation methods the technique is based upon the simple fact that a chemical substance shows marked selective absorption in the IR region. After absorption of IR radiation the molecules of chemical substance vibrates at many rates of vibration, giving rise to close packed absorption bands, called IR absorption spectrum which may prolonged over wide wavelength range. Different bands will be present in IR spectrum which will correspond to the characteristic functional groups and bonds present in a chemical substance. Thus, an IR spectrum of a chemical substance is a fingerprint for its identification.

## III. CHARACTERIZATION OF LOSARTAN POTASSIUM BUCCAL PATCH

*A. Physical appearance*

All the Buccal patches were visibly inspected for Transparency, Stickiness, flexibility and smoothness.

*B. Weight Uniformity*

It was determined by weighing three film formulations individually on a digital balance (Shimadzu). The average value was taken as a weight of the films.

*C. Thickness uniformity*

The thickness of the drug loaded patch is measured in different point by using a Vernier caliper and determines the average thickness and standard deviation for the same to ensure the thickness of the prepared patch.

*D. Folding endurance*

A strip of film (2x 2 cm) was cut evenly and repeatedly folded at the same place till it broke. The number of times the film could be folded at the same place without breaking gave the value of the folding endurance.

*E. Drug content*

The patches (1 $cm^3$) were cut and added to a volumetric flask containing 10 ml of phosphate buffer of pH 7.4 (solution) from this solution 0.1 ml solution was taken and the volume was made (20 ml) with phosphate buffer saline (pH 7.4). The contents were filtered using What man filter paper and the filter was examined for the drug content against the reference solution consisting of phosphate buffer (contains no drug) at 227 nm spectrophotometrically.

*F. In vitro drug release through cellophane membrane.*

The drug release profile from buccal films was performed by using Franz diffusion cell. This patch was placed on cellophane membrane mounted between the donor and receptor compartment of the diffusion cell.The receptor chamber was filled with freshly prepared PBS (pH 7.4) solution to solubilize the drug. By using magnetic stirrer stir the receptor chamber The samples (1.0 ml aliquots) were collected at suitable time interval. Samples were analyzed for drug content by UV visible spectrophotometer at 227 nm after appropriate dilutions Cumulative corrections were made to obtain the total amount of drug release at each time

ISSN No:-2456-2165

interval. The cumulative amount of drug released across the cellophane membrane was identified as a function of time.

*G. Stability Study.*

The batch F4 was selected as an optimum batch for the stability study. The stability study was at accelerated conditions of 40°C/5% RH conditions for the period of one month. Three films are individually wrapped using aluminum foil and kept at the specific conditions of 40°C/5% RH for the period of one month the remaining parameters were kept same as kept in diffusion study and diffusion profile was analyzed after one month.

| Properties | Observation | Result |
|---|---|---|
| Colour | White | White |
| Taste | Bitter | Bitter |
| Appearance | Crystalline powder | Crystalline powder |
| Melting Point | $265^0$C -$266^0$C | $265^0$C$\pm$ 1 $^0$C |

Table 2: Organoleptic characteristics

## IV. RESULT AND DISCUSSION

The buccal patch Losartan potassium by solvent casting technique were found to be satisfactory

*A. Spectroscopic analysis:*

a) Determination of lambda max

The standard solution of Losartan potassium of concentration 10 µg/ml showed maximum absorbance at the wavelength of 227 nm (Fig No. 8.1). Hence the 2, max of Losartan potassium was found to be 227 nm.

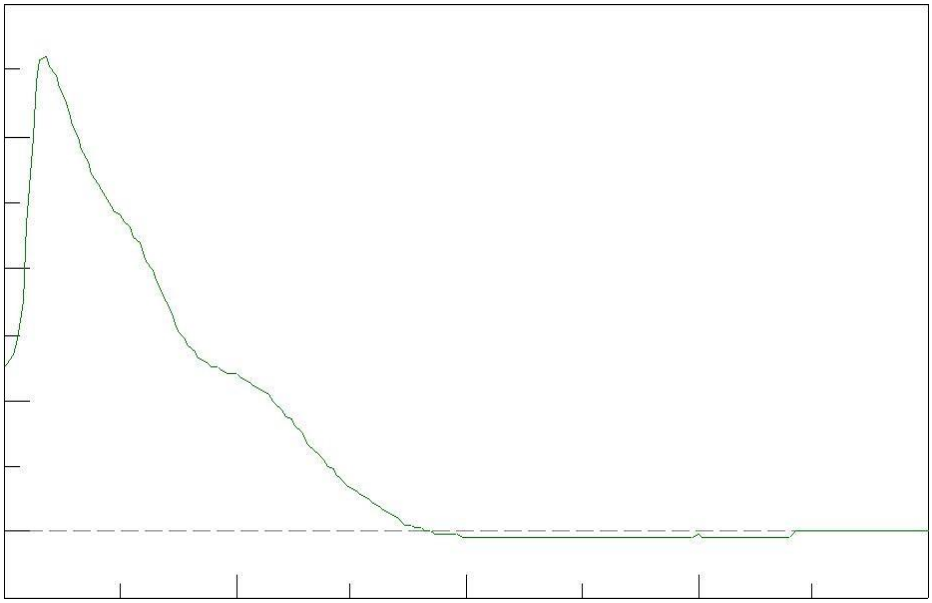

Fig. 1: Uv-visible Spectrum of Losartan Potassium.

*B. Calibration curve of Losartan potassium*

Losartan potassium in phosphate buffer showed straight line (Fig No. 8.2.) which passes from origin. The Beer's Lambert's law was found to be obeyed over the range of 0-5ug /ml. The data for calibration curve shown in Table no.8.1.

| **Concentration of Losartan Potassium (µg/ml)** | **Absorbance at 227 nm** |
|---|---|
| **0** | **000** |
| **1** | **0.041** |
| **2** | **0.079** |
| **3** | **0.112** |
| **4** | **0.151** |
| **5** | **0.191** |
| | |

Table 3: Data for Calibration Curve of Losartan Potassium in Phosphate Buffer

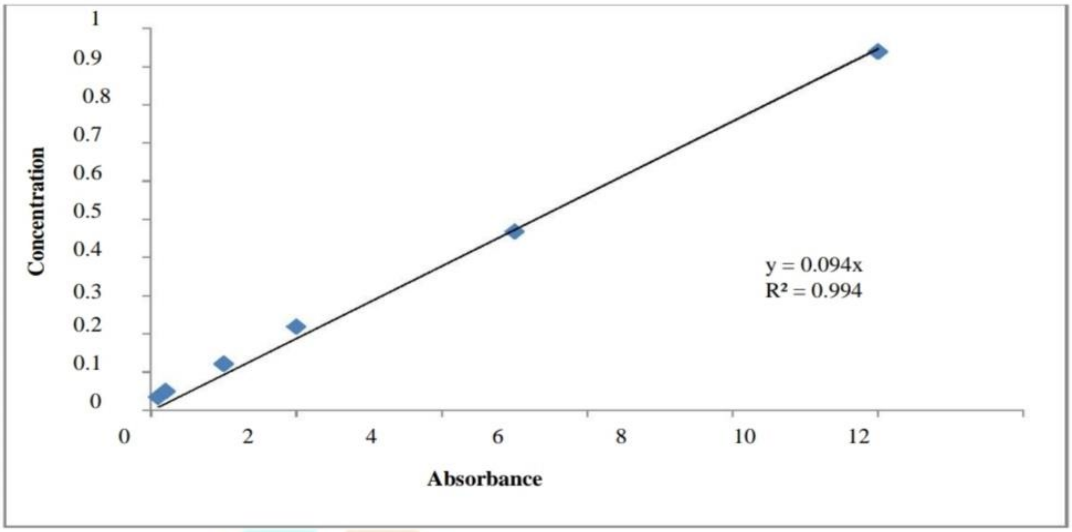


Fig. 2: Calibration Curve of Losartan Potassium in Phosphate Buffer at 227nm

The details of calibration curve are as given below:
Linear regression Equation is, **Y = Mx + c**

Where, Y absorbance.
M-slope
x= concentration and
c=intercept.

Interpreted the calibration curve equation obtained was
**y=0.094x+0.001**
The value of slope (m) is 0.094.
The value of intercept (c) is 0.001.
The value of regression coefficient (R) is 0.999.

*C. Compatibility study between drug and polymers:*

In FTIR spectra of Losartan potassium (Fig No. 8.3.), all the essential peaks were found to be present, which confirmed the purity of sample. Table No. 8.2 Display peaks observed at various wave numbers and the functional group associated with these peaks for drug FTIR spectra of Losartan potassium pure (Figure 8.3) drug displayed principal bands at wave number of 3185.83 cm-1 hydroxyl group (O-H), 2952.48 cm-1 for CH stretching in aromatic ring 2868 59 cm-1for CH stretching in aliphatic ring, 1574.59 cm 1 for carbonyl group(C-O) in carboxylic acid function group,1456.06 cm-1 for C-C stretching in aromatic ring, 1256.4 cm-1 for C-O-C(ether linkage), 909 208 cm-1 for AR CH(out plane bending).

- **Figures:**

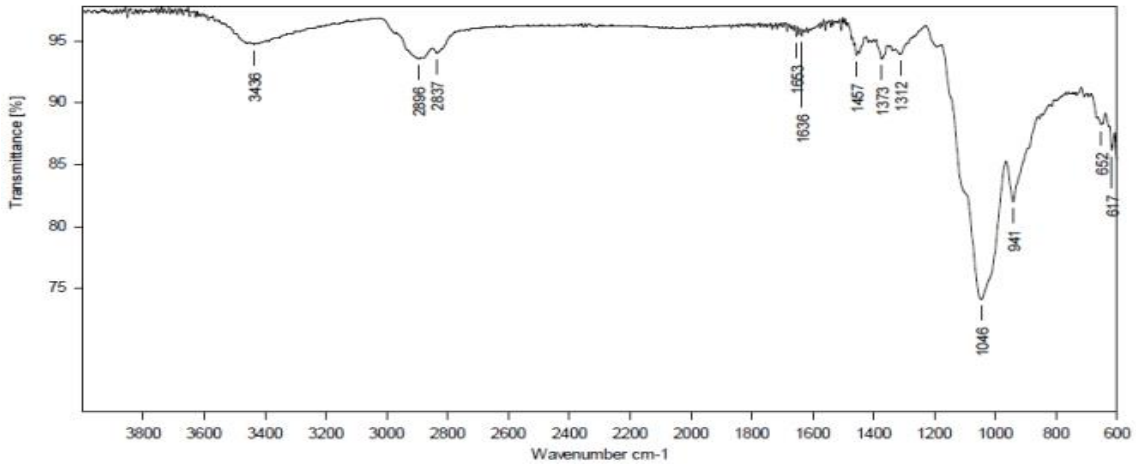


Fig. 3: FTIR Spectroscopy of losartan Potassium

ISSN No:-2456-2165

| Sr. no. | Peak Position | Functional Group |
|---|---|---|
| 1 | 3436 | OH |
| 2 | 2895 | CH Stretching |
| 3 | 2837 | CH Aliphatic |
| 4 | 1636 | C=O |
| 5 | 1457 | C=C Stretching |
| 6 | 1312 | C-O-C Ether Linkage |
| 7 | 1045 | Ar-CH bending |

Table 4: Interpretation of IR Spectra of Losartan Potassium

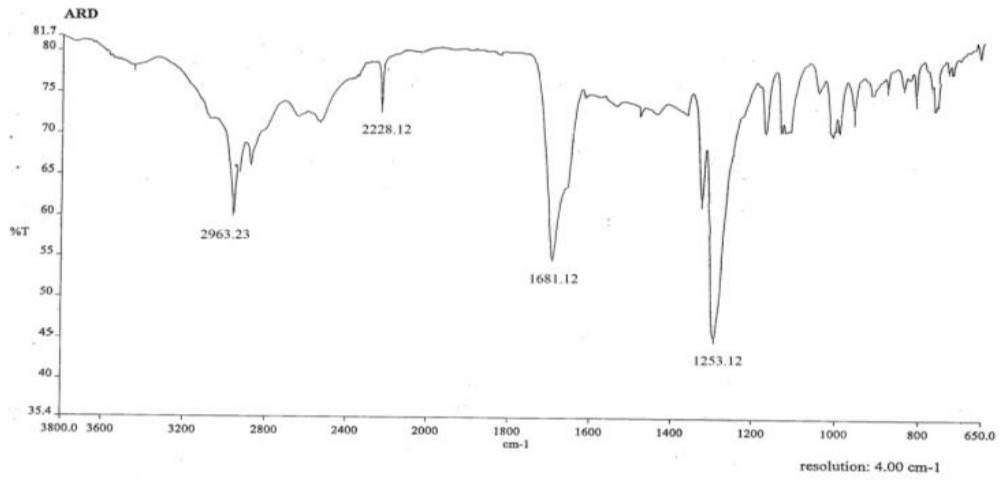


Fig. 4: FTIR Spectroscopy of HPMC

| Sr. no. | Peak Position | Functional Group |
|---|---|---|
| 1 | 2963 | C=C Stretching |
| 2 | 2228 | CH |
| 3 | 1681 | OH Stretching |
| 4 | 1253 | C-O-C |
| 5 | 1347 | O-H Bending |

Table 5: Interpretation of IR Spectra HPMC

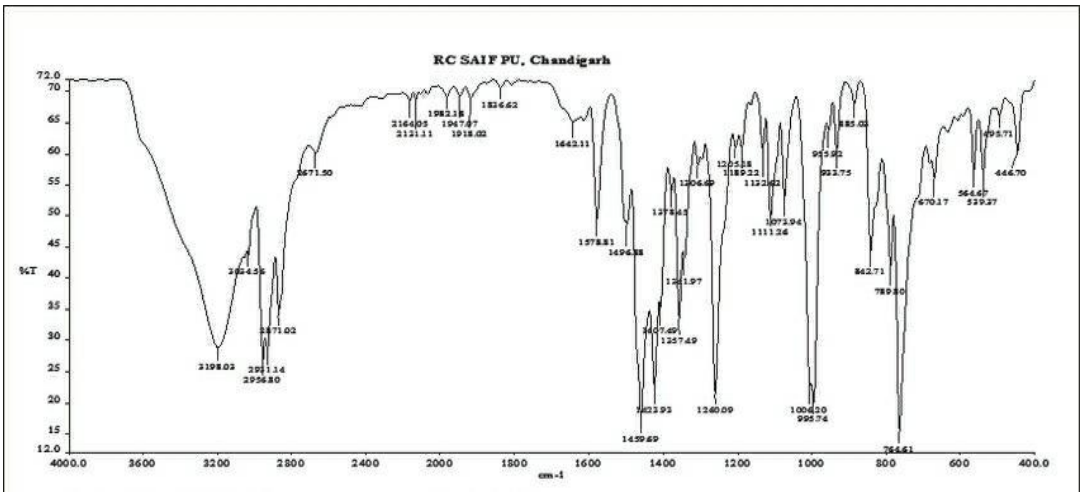


Fig. 5: FTIR Spectroscopy of EC

| Sr.no. | Peak Position | Functional Group |
|---|---|---|
| 1 | 1373.07 $cm^1$ | OH |
| 2 | 1201.43$cm^1$ | C-O-C Stretching |
| 3 | 1051.58$cm^1$ | CH Bending |

Table 6: Interpretation of EC

ISSN No:-2456-2165

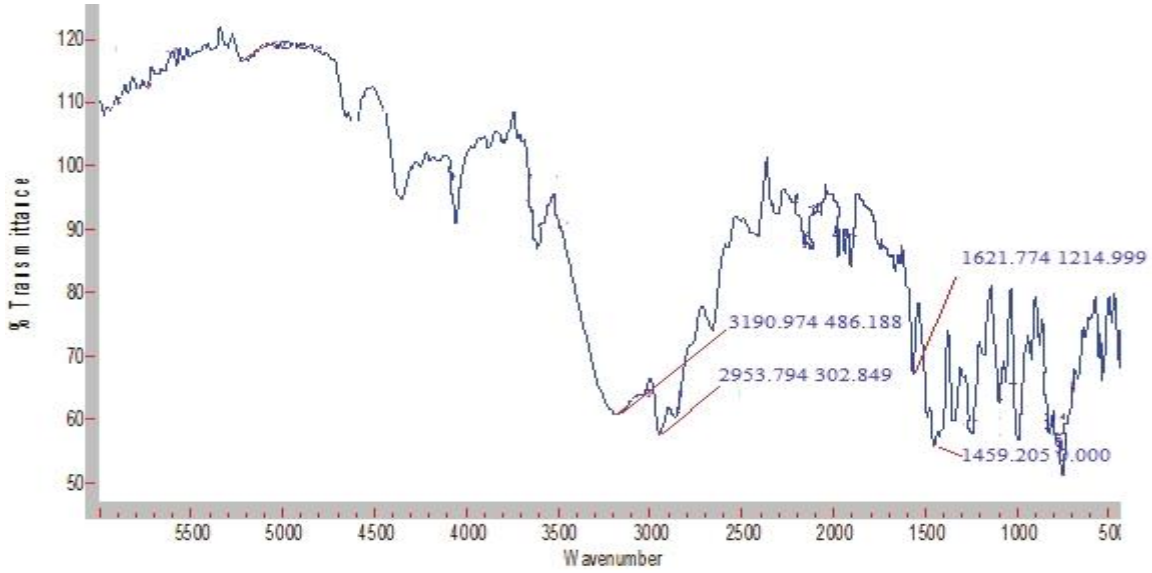


Fig. 6: FTIR Spectroscopy of Eudragit L100+ Drug

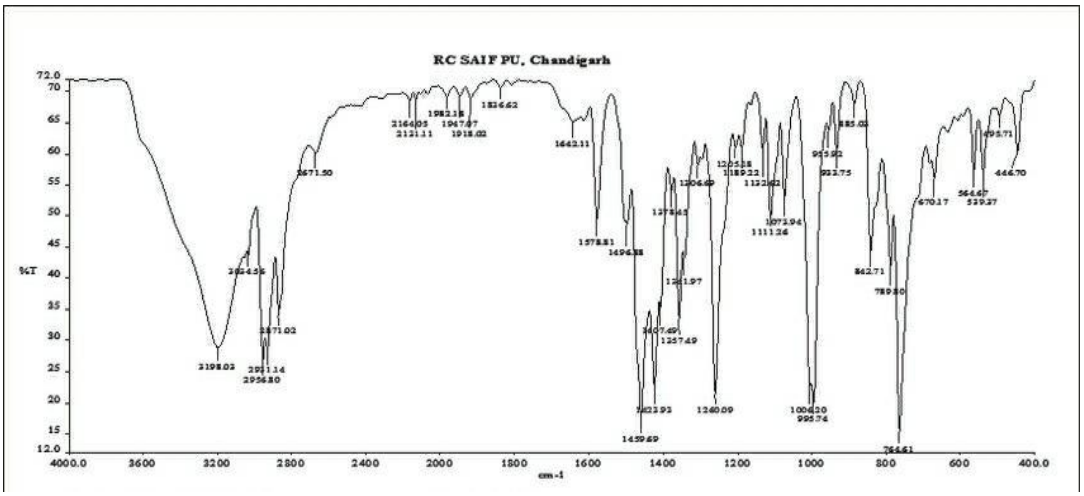


Fig. 7: FTIR EC+ Drug

If the drug and the polymer would connect, then the functional groups in the FTIR spectra would show band shifts and broadening correlated to the spectra for the pure drug and polymer. The FTIR spectra gained from the various polymers showed peaks which were a summation of the characteristic peaks gained with the pure drug and pure carriers and spectra's can be simply regarded as the superposition of those of Losartan potassium and carriers. No chemical interaction showed of the drug.

| Sr. No | Batch Code | Weight (mg) | Thickness (mm) | Folding Endurance |
|---|---|---|---|---|
| 1 | F1 | 360.5 | 0.065 | >300 |
| 2 | F2 | 420.8 | 0.082 | >300 |
| 3 | F3 | 490.6 | 0.094 | >300 |
| 4 | F4 | 365.5 | 0.066 | >300 |
| 5 | F5 | 430.6 | 0.134 | >200 |

Table 7: Physical Parameter and Folding Endurance in Films of Losartan Potassium

| Batch Code | Drug Content (%) |
|---|---|
| F1 | 88.00% |
| F2 | 90.16% |
| F3 | 92.00% |
| F4 | 94.70% |
| F5 | 89.29% |

Table 8: Data for Content Uniformity

ISSN No:-2456-2165

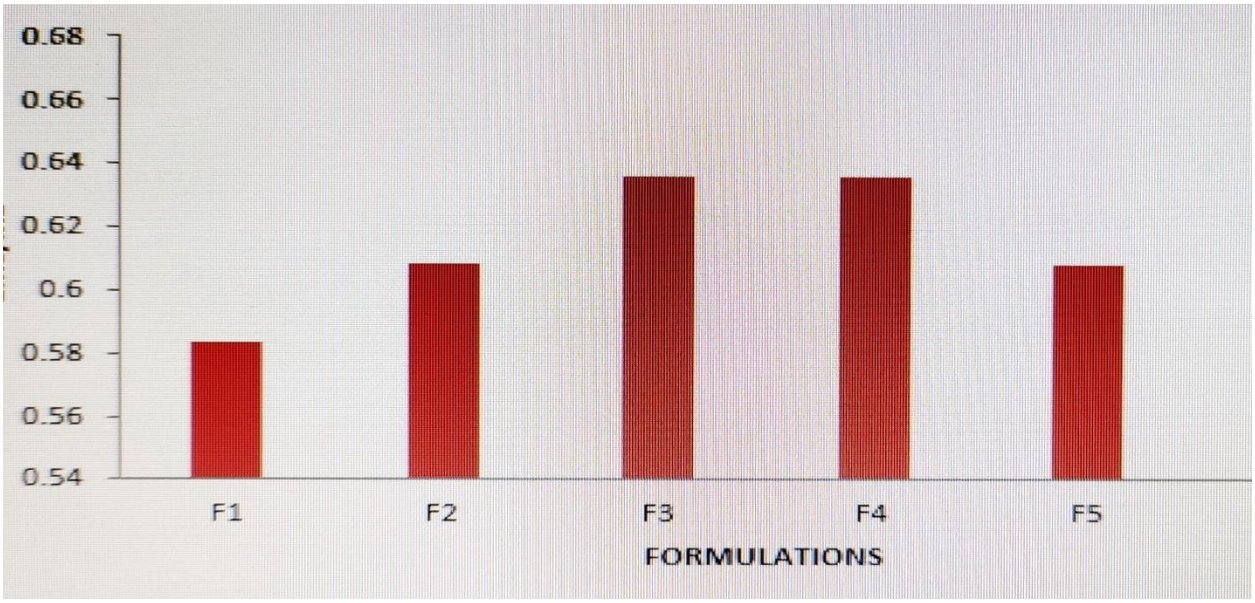


Fig. 8: 8.8% Total Drug Content of Batches

| Time (hr) | F1 | F2 | F3 | F4 | F5 |
|---|---|---|---|---|---|
| | Cumulative release of Drug % | Cumulative release of Drug % | Cumulative release of Drug % | Cumulative release of Drug % | Cumulative release of Drug % |
| 1 | 11.99 | 12.16. | 15.27 | 15.80 | 11.17 |
| 2 | 46.20 | 31.06 | 36.08 | 37.68 | 39.92 |
| 3 | 51.10 | 45.4 | 53.18 | 42.13 | 61.13 |
| 4 | 78.12 | 74.70 | 86.20 | 76.13 | 79.9 |
| 5 | 92.16 | 91.05 | 90.11 | 95.13 | 88.16 |

Fig. 9: Cumulative % Drug Release

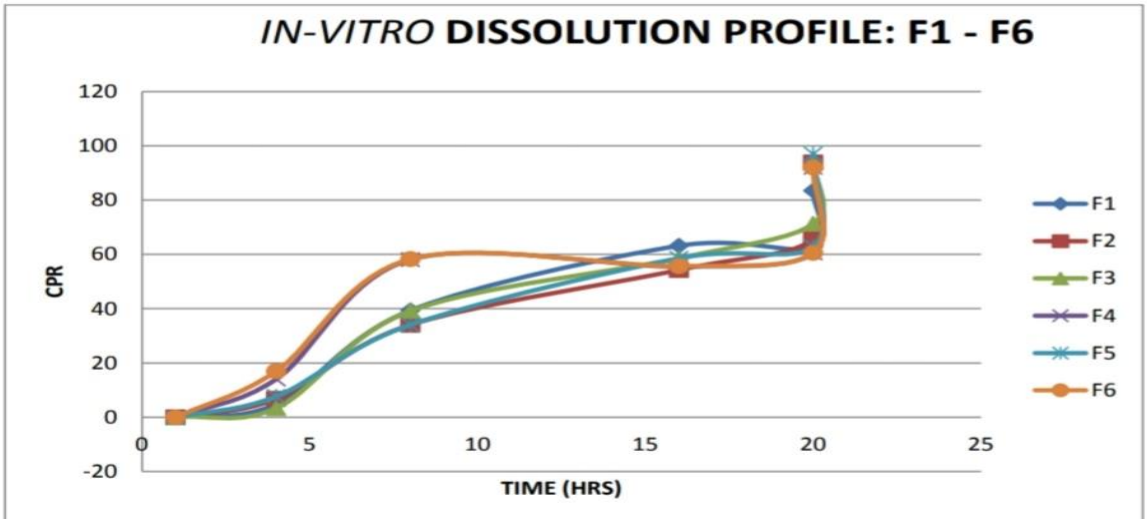


Fig. 9:

| Test Parameter | Initial | After 1month at 40.C 5% RH |
|---|---|---|
| Physical Appearance | Opaque Non Sticky Flexible Smooth | Opaque Non Sticky Flexible Smooth |
| Weight Uniformity | 365.5 | 362.3 |
| Thickness | 0.066 | 0.064 |
| Folding Endurance | >300 | >300 |
| Drug Release study | 95.13 | 93.78 |
| Drug content | 94.70 | 93.20 |

Table 10: Stability Study

ISSN No:-2456-2165

## V. SUMMARY AND CONCLUSION

Recently the buccal patch has been increasingly used for administration of drug cause drug with shortened half-life which cause non-compliance by reason of frequent dosing and say eliminate of film from the site.

In the present research work we have prepared Losartan potassium buccal patch with n objective of improving bioavailability of Losartan potassium. Buccal patches was formulated by solvent casting method using HPMC, Ethyl cellulose and Eudragit 1.100 in different concentrations.Amidst the different polymeric combinations, the combination F4 was establish to be most suitable. The batch F4 combinations polymers namely Eudragit L 100 and Ethyl cellulose in 2:1 ratios achieved the requirement of aexcellent buccal film and showed best folding endurance. It also exhibited in vitro residence time up to 5 h. It pursue in vitro drug release up to 95.13% for 5 h.So, from the current study it can be achieved that, buccal drug delivery system for Losartan potassium with Eudragit L 100 and Ethyl cellulose meet the optimal requirement for buccal devices which can be excellent way to bypass the extensive hepatic first pass metabolism and inhance the bioavailability.

## REFERENCES


[1.] Sanghi D. Rakesh T. An overview on buccal drug delivery system. International Journal of Pharmacotherapy 2015, 5(1), 8-16.

[2.] Verma N. Chattopadhyay P. Preparation of mucoadhesivebuccal patches of carvedilol and evaluation for in-vitro drug permeation through porcine buccal membrane. African Journal of Pharmacy and Pharmacology2011, 5(9), 1228-1233.

[3.] Shubhra P. Formulation and evaluation of buccal patches of diclofenac Sodium. International Journal of Scientific and Engineering Research 2012, 3(12), 1-7.

[4.] Patel AR, Patel DA, Chaudhry SV. Mucoadhesivebuccal drug delivery system. International Journal of Pharmaceutical and Life Science2011, 2(6), 848-856

[5.] Revathi N, Mettu SR. Buccalpatch as drug delivery system: an overview. International Journal of Current Pharmaceutical Research2013, 5(2), 40-47.

[6.] Harshad GP, Janak JJ. Buccal patch: a technical note. International Journal of Pharmaceutics2001, 213(1), 25-29.

[7.] Ilango R, Kavimani S, Mullaicharan R, Jayakar B. In vitro studies on buccal strips of Glibenclamide using chitosan Indian Journal of Pharmaceutical Sciences 1997, 59(5), 2323.

[8.] Navpreet K. Design, developmentand evaluation of mucoadhesivepatches of losartan for buccal delivery European Journal of Pharmaceuticaland Medical Research2014, 1(1), 105-126.

[9.] Sumedha B, Mayank B Formulation and evaluation of fast dissolving film of an antihypertensive drug International Journalof Pharmaceutical, Chemical and Biological Sciences2013, 3(4), 1097-1108.

[10.] Sumangala D. Sellappan V. Buccal penetration enhancers-an overview. Asian journals of Pharmaceutical and Clinical Research, 2013, 6(3), 136-147.

[11.] Surrenders V. Mahakam, Aruna R. Sana S. An overview on buccal drug delivery system. International Journal of Pharmaceutical Sciences and Research 2011, 2(6), 1303 1320

[12.] Katrin M, Katrin K. Atari N, Yogeshwar NK, Richard HG, Passive skin permeations enhancement and its qualification inventor. European Journal of Pharmaceutics and Biopharmaceutics 2001.52(4), 103-112

[13.] Prasanna P. Souvik D.Effect of permeation enhancers on boccal patches of propranolol hydrochloride for boccal drug delivery International Journal of Innovative Pharmaceutical Sciences and Research2013.1 (1), 117-131.

[14.] Gandhi RB, Robinson JR., Oral cavity as a site for bioadhesive drug delivery Advanced Drug Delivery Reviews 1994, 13(2), 43-74. 15) Amir HS Buccal mucosa as a route for systemic drug delivery: a review. Journal of Pharmacy and Pharmaceutical Science 1998, 1(1), 15-30.

[15.] Dhaval AP, Patel MR. Buccal mucosa as a route for systemic drug delivery a review International Journal of Drug Development and Research 2012.4(2), 99-116.

[16.] Trophimus GJ. The effect of drugs in the oral cavity: a review. Journal of Pharmaceutical Science and Reseach2014, 6(2), 89-96.

[17.] Rudolph S. The structure and function of oral mucosa. Journal of Anatomy 1985, 140(4), 719-720 Nishan NB, Sandeep C A review on buccal drug delivery system. International.