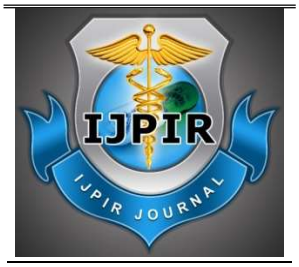
Research Article



ISSN Print 2231 – 3648
Online 2231 – 3656

Available Online at: www.ijpir.com

International Journal of Pharmacy and Industrial Research

FORMULATION AND EVALUATION OF RAMIPRIL TRANSFEROSOMAL GEL

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ABSTRACT

In the present work an attempt was being made to formulate and evaluate topical gel containing Ramipril. Carbopol 971, Sodium CMC and Carbopol 934 were selected as polymers. The drug and excipient compatibility was studied by using FTIR. Nine formulations of gels were prepared by taking different quantities of polymers. The prepared gel was subjected to various evaluation tests like pH, Spreadability, viscosity, content uniformity and diffusion studies conducted up to 12 hrs. All the results were within the limits; by diffusion studies it was observed that formulation F7 shown maximum drug release of 95.49% which was considered as optimized formulation.

Keywords: Ramipril, Topical, Carbopol 971, Sodium CMC and Carbopol.

INTRODUCTION

TOPICAL DRUG DELIVERY SYSTEMS

Topical preparations are used for the localized effects at the site of their application by virtue of drug penetration into the underlying layers of skin or mucous membranes. The main advantage of topical delivery system is to bypass first pass metabolism. Avoidance of the risks and inconvenience of intravenous therapy and of the varied conditions of absorption, like pH changes, presence of enzymes, gastric emptying time are other advantage of topical preparations. Semi-solid formulation in all their diversity dominate the system for topical delivery, but foams, spray, medicated powders, solution and even medicated adhesive systems are in use. The topical drug delivery system is generally used where the others system of drug administration fails or it is mainly used in pain management, contraception, and urinary incontinence. Over the last decades the

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treatment of illness has been accomplished by administrating drugs to human body via various routes namely oral, sublingual, rectal, parental, topical, inhalation etc. Topical drug delivery can be defined as the application of a drug containing formulation to the skin to direct treat cutaneous disorders (e.g. acne) or the cutaneous manifestations of a general disease (e.g. psoriasis) with the intent of confining the pharmacological or other effect of the drug to the surface of the skin or within the skin. Topical activities may or may not require intra-cutaneous penetration or deposition. Topical drug delivery systems include a large variety of pharmaceutical dosage form like semisolids, liquid preparation, sprays and solid powders. Most widely used semisolid preparation for topical drug delivery includes gels, creams and ointments.

Topical formulations have three main functions:

- To help hydrate skin because of their emollient properties.
- To protect from external environment or heal an intact or injured area of the skin.
- To deliver medication to the skin.

STRUCTURE OF GELS

A gel consists of a natural or synthetic polymer forming a three dimensional matrix throughout a dispersion medium or hydrophilic liquid. After application, the liquid evaporates leaving the drug entrapped in a thin film of the gel-forming matrix physically covering the skin. The presence of a network formed by the interlocking of particles of the gelling agent gives rise to the rigidity of a gel. The nature of the particles and the type of form that is responsible for the linkages determine the structure of the network and the property of the gel.

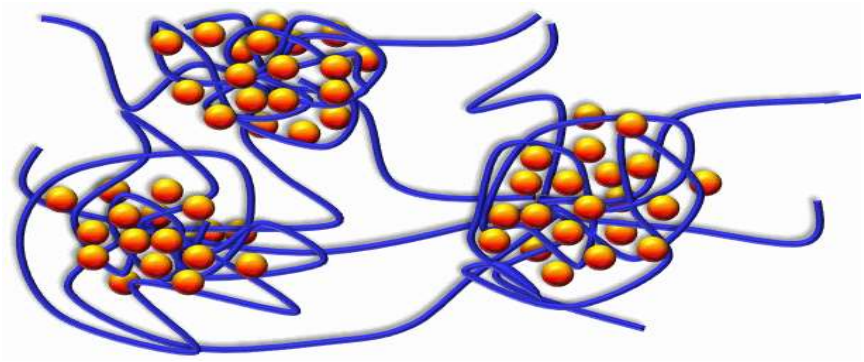

Figure 1: Structure of a gel

ADVANTAGES OF TOPICAL DRUG ADMINISTRATION

- Avoids gastrointestinal (GI) drug absorption difficulties caused by GI pH, enzymatic activity and drug interactions with food, drink, and other orally administered drugs.
- A substitute for other routes of administration (e.g. oral administration, intravenousinjection) when that route is unsuitable, as with vomiting, swallowing problems, resistant children and diarrhoea.
- Patient acceptability is better as this drug delivery system is non-invasive, avoiding the inconvenience of parenteral therapy.
- Avoids the first-pass effect, possibly avoiding the deactivation by digestive and liver enzymes. Reduction of doses as compare to oral dosage forms.
- Provides extended therapy with a single application, improving compliance.
- Drug therapy may be terminated rapidly by removal of the application from the skin surface.

- Less greasy and can be easily removed from the skin.

AIM

The aim of the present study is to formulate and evaluate topical gel containing Ramipril asmodel drug.

OBJECTIVE OF THE STUDY

Following are the objectives of the present study

- To formulate Ramipril gels using different bases.
- To improve diffusivity of Ramipril across skin layers by using suitable penetrationenhancers in the formulation.
- To evaluate the formulated dosage forms for their pharmaceutical properties

MATERIALS AND METHODS

PREPARATION OF RAMIPRIL

Table.1: Composition of different Emulgel formulations

Formulation (F)	Drug (mg)	Carbopol 971 (mg)	Sodium CMC	Carbopol 934 (mg)	Methanol (ml)	Triethanol amine (ml)	Poly ethylene glycol (mg)	Methyl paraben (mg)	Water
F1	02	500	-	-	10	5	10	5	Q.s
F2	02	1500	-	-	10	5	10	5	Q.s
F3	02	2000	-	-	10	5	10	5	Q.s
F4	02	-	500	-	10	5	10	5	Q.s
F5	02	-	1500	-	10	5	10	5	Q.s
F7	02	-	2000	-	10	5	10	5	Q.s
F7	02	-		500	10	5	10	5	Q.s
F8	02	-		1500	10	5	10	5	Q.s
F9	02	-		2000	10	5	10	5	Q.s

Preparation of Ramipril gel

Above mentioned quantity of carbopol 934, Carbopol 971was soaked in water for a period of 2 hours. Carbopol was then neutralized with triethanolamine (TEA) with stirring. Then specified amount of drug was dissolved in appropriate and preweighted amounts of propylene glycol and ethanol. Solvent blend was transferred to carbopol container and agitated for additional 20 min. The dispersion was then allowed to hydrate and swell for 70 min, finally adjusted the pH with 98% TEA until the desired pH value was approximately reached (7.8-7). During pH adjustment, the mixture was stirred gently with a spatula until homogeneous gel was formed. All the samples were allowed to equilibrate for at least 24 hours at room temperature prior to performing rheological measurements.

RESULTS AND DISCUSSIONS

ANALYTICAL STUDY

Scanning of drug

Ramipril pure drug was scanned in methanol between 200 nm and 400 nm using ultraviolet spectrophotometer. Ramipril was identified by its light absorption pattern which follows the absorption of light in the range 220 to 400 nm and a maximum absorbance at about 210 nm. A broad shoulder at about 210 nm was observed which confirm the presence of Ramipril. Ramipril gave highest peak at 210 nm and the same was selected for further evaluations.

Calibration curve in water (make up with pH 6.8 phosphate buffer)

Standard solutions of different concentrations were prepared and their absorbance was measured at 288 nm. Calibration curve was plotted against drug concentrations versus absorbance as given in the (Figure).

Table.2: Determination of λmax of Ramipril in methanol-λmax = 210 nm

Concentration (µg /ml)	Absorbance
0	0
2	0.139
4	0.258
6	0.391
8	0.501
10	0.616
12	0.834

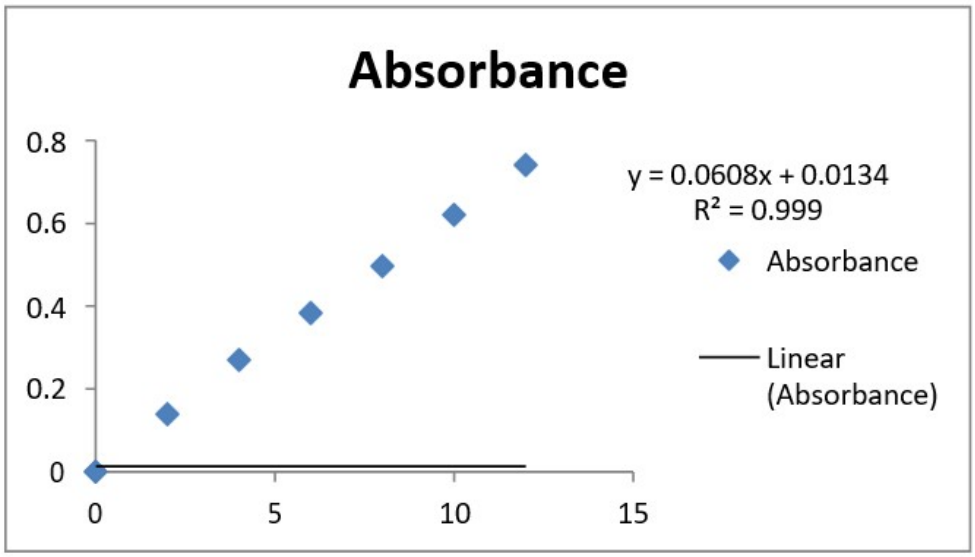

Figure 2: Standard graph of Ramipril

CHARACTERIZATION OF GELS

Percentage yield

Table 3: Percentage yield of gel formulations

Sl.no	Formulation	Percentage yield
1	F1	90.54
2	F2	95.68
3	F3	93.48
4	F4	92.33
5	F5	93.85
6	F6	94.28
7	F8	91.22
8	F8	95.89
9	F9	91.33

Drug content

Table 4: Drug content of gel formulations

Sl.no	Formulation	Drug content
1	F1	92
2	F2	96
3	F3	91
4	F4	95
5	F5	94
6	F6	93
7	F8	92
8	F8	98
9	F9	94

Viscosity

Table 5: Viscosity of gel formulations

Sl.no	Formulation	Viscosity (cps)
1	F1	63,540.06
2	F2	91,669.03
3	F3	92362.38
4	F4	1,19,000.01
5	F5	1,35,688.30
6	F6	61,552.01
7	F8	99,882.04
8	F8	1,28,023.08
9	F9	98,489.04

pH measurement

Table 6:pH of gel formulations

Sl.no	Formulation	pH
1	F1	6.8
2	F2	8
3	F3	6.4
4	F4	6.2
5	F5	6.8
6	F6	8.1
7	F8	6.8
8	F8	6.4
9	F9	6.9

Spreadability studies

Table 7: Spreadability values of gel formulation

Sl.no	Formulation	Spreadability gm.cm^2
1	F1	11.06
2	F2	11.96
3	F3	10.82
4	F4	11.88
5	F5	10.58
6	F6	11.10
7	F8	10.84
8	F8	11.65
9	F9	11.09

IN-VITRO RELEASE STUDIES

Table-8. *In-vitro* cumulative % drug release profile for Ramipril

Time	Cumulative % drug release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
30min	13.56	18.5	11.09	18.09	12.39	12.01	10.21	3.11	5.54
1hr	24.55	33.52	19.26	32.51	22.21	18.09	20.62	8.15	12.18
2hr	31.86	35.3	25.21	38.42	26.22	25.31	30.82	14.21	24.58
3hr	34.22	40.52	31.81	46.42	32.09	29.69	33.32	28.54	33.19
4hr	39.26	45.81	35.21	50.31	35.21	31.03	38.29	35.45	39.89
5hr	41.62	55.32	39.05	56.51	38.02	33.61	40.25	45.21	48.69
6hr	44.82	59.5	45.02	59.41	43.3	35.3	44.91	53.88	52.85
8hr	49.25	62.32	49.05	61.21	48.31	41.65	52.41	59.34	61.38
8hr	53.45	66.92	55.51	65.82	49.85	43.32	58.86	66.83	68.54
9hr	60.53	80.08	59.38	82.46	55.31	48.32	59.92	88.69	85.28
10hr	68.02	85.41	68.42	88.32	65.21	51.09	62.59	85.54	89.19
11hr	83.52	89.2	81.31	85.31	69.81	56.31	65.43	91.15	81.14
12hr	86.89	82.41	84.62	88.42	83.09	65.21	68.19	95.49	86.68

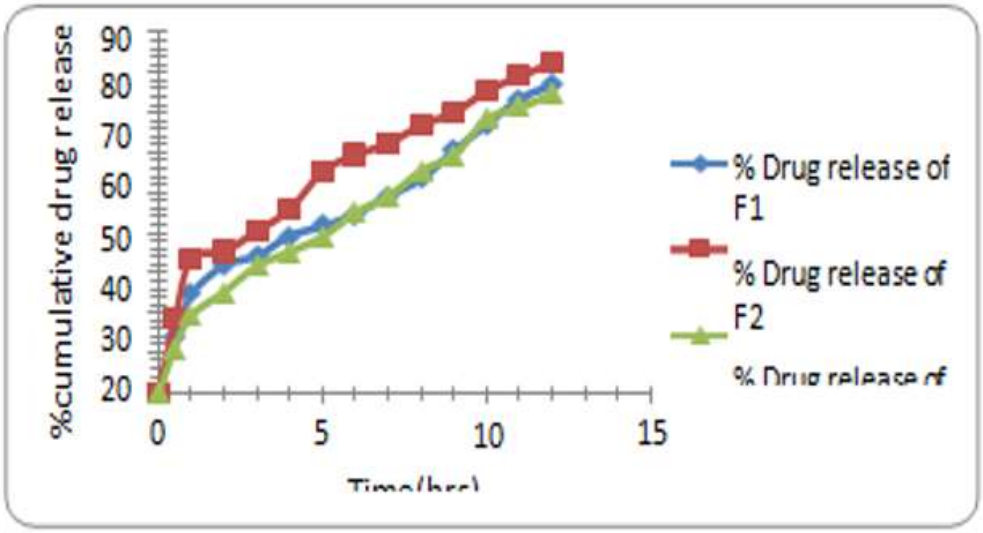

Fig. 3. Dissolution graphs for the formulations F1, F2, F3

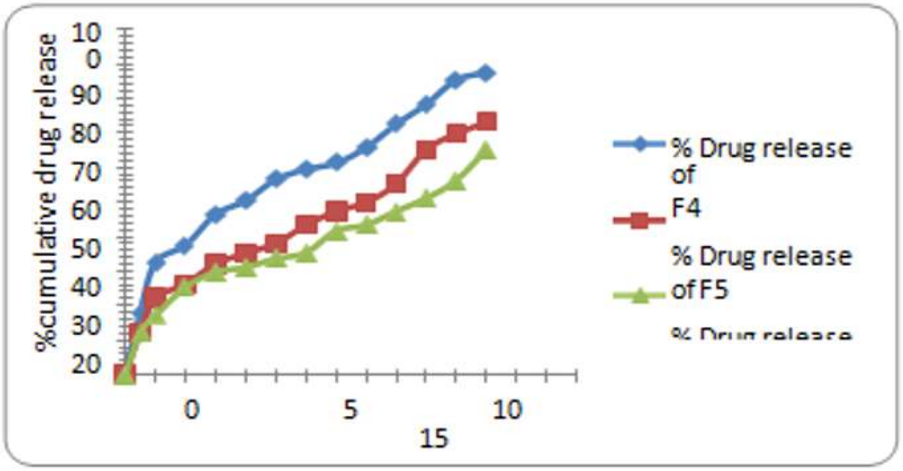

Fig: 4. Dissolution graphs for the formulations F4, F5, F6

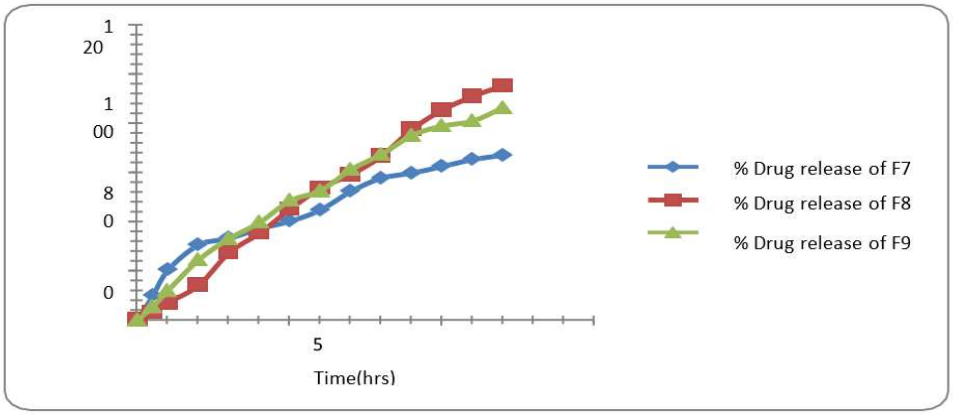

Fig : 5.Dissolution graphs for the formulations F8,F8,F9

Table : 9. Release kinetics

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT(T)	LOG (%) RELEASE	LOG(T)	LOG (%) REMAIN
0	0	0			2.000
3.11	0.5	0.808	0.493	-0.301	1.986
8.15	1	1.000	0.854	0.000	1.968
14.21	2	1.414	1.153	0.301	1.933
28.54	3	1.832	1.440	0.488	1.860
35.45	4	2.000	1.550	0.602	1.810
45.21	5	2.236	1.655	0.699	1.839
53.88	6	2.449	1.831	0.888	1.665
59.34	8	2.646	1.883	0.845	1.609
66.83	8	2.828	1.824	0.903	1.522
88.69	9	3.000	1.890	0.954	1.348
85.54	10	3.162	1.932	1.000	1.160
91.15	11	3.318	1.960	1.041	0.948
95.49	12	3.464	1.980	1.089	0.654

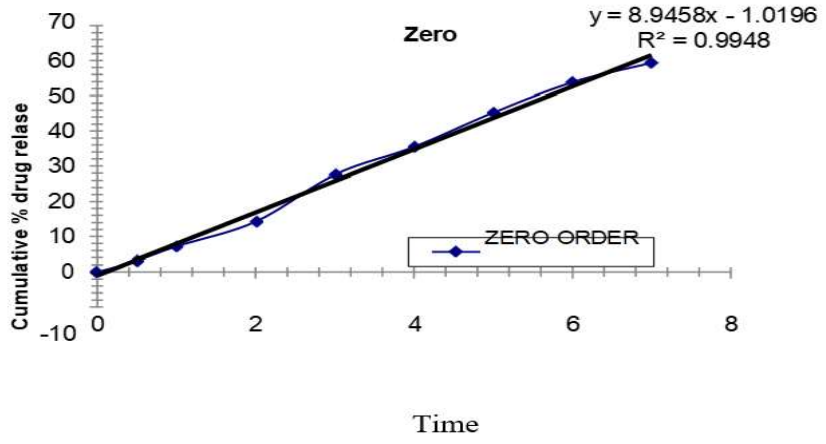

Fig.6: kinetic model zero order

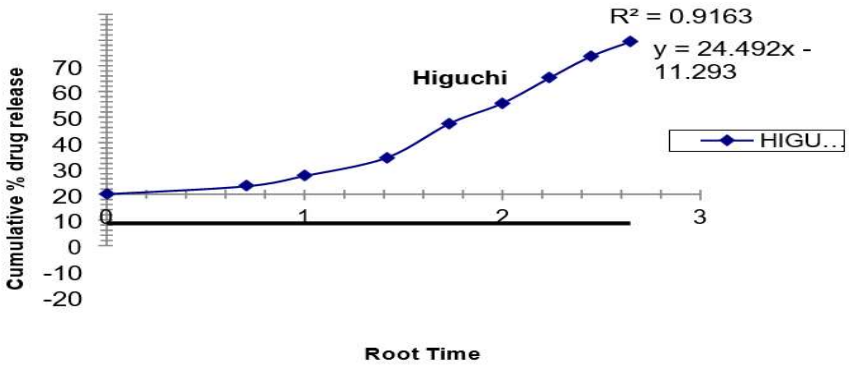

Fig :7 kinetic model-higuchi

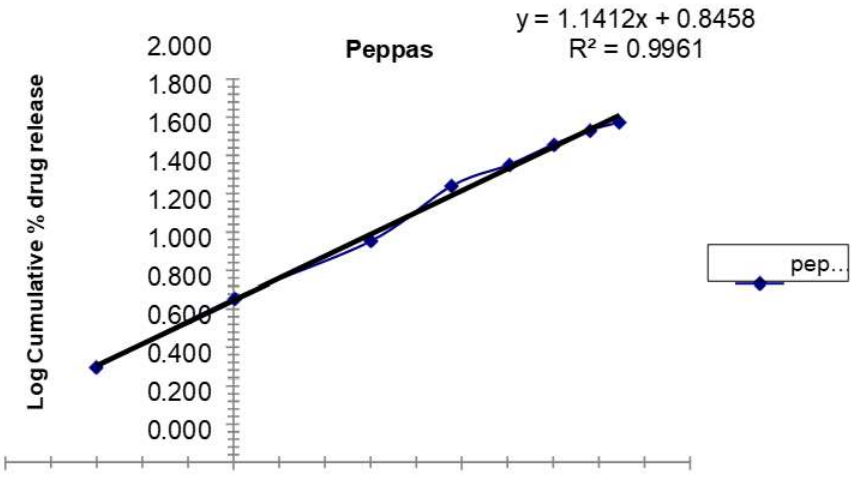

Fig : 8 kinetic model-peppas

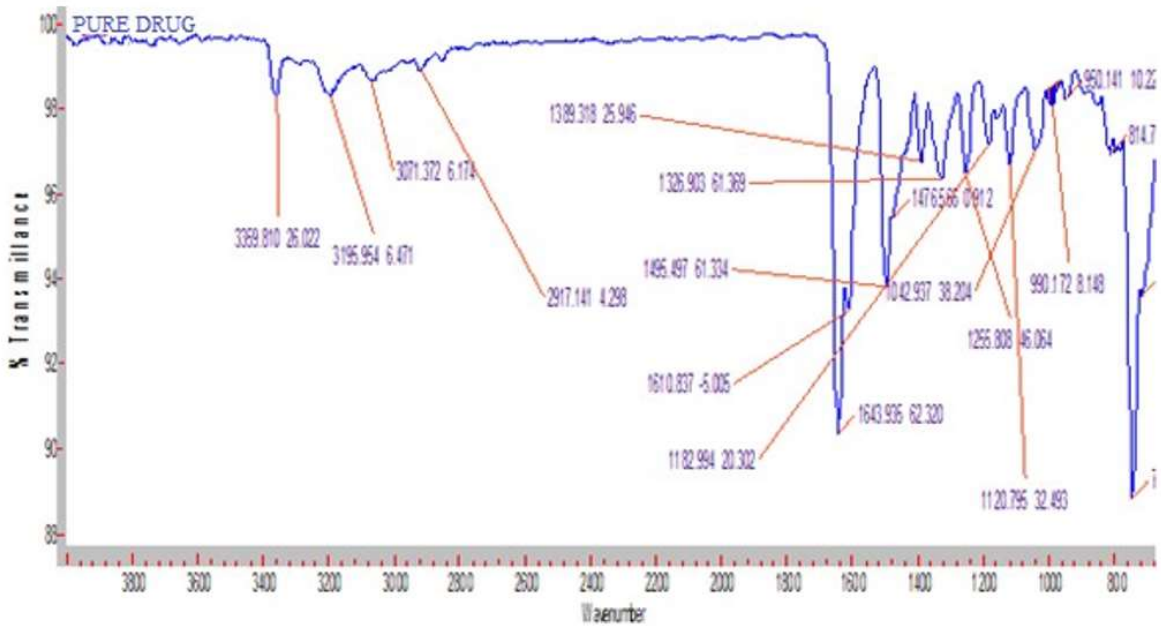

Fig 9: FTIR Spectrum of Pure Drug

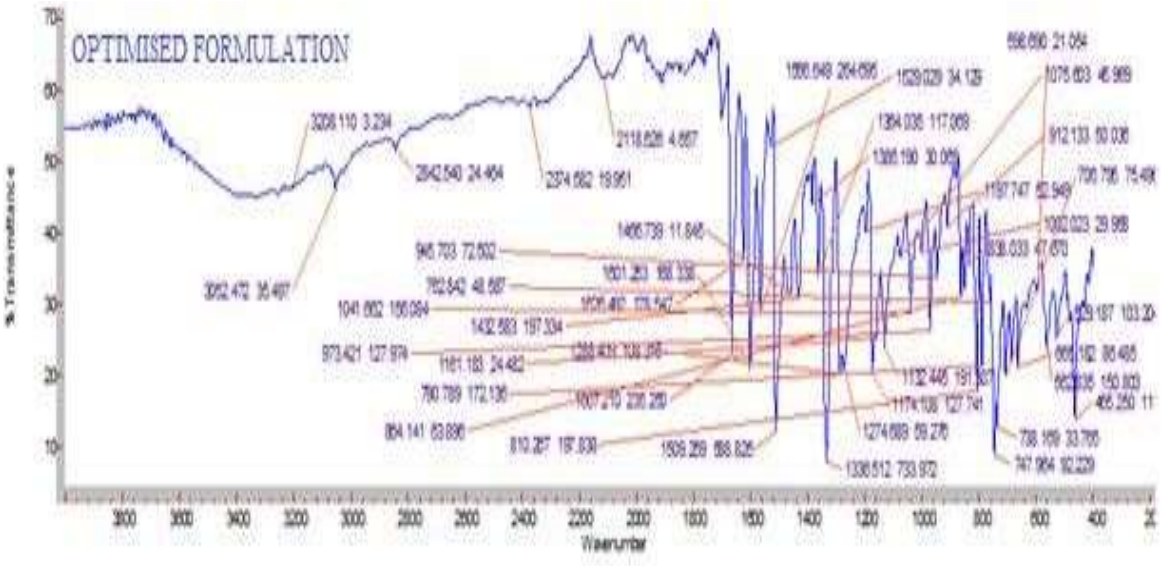

Fig 10: FTIR Spectrum of optimized formulation

SUMMARY AND CONCLUSION

- In the present work an attempt was being made to formulate and evaluate topical gel containing Ramipril.
- Carbopol 971, Sodium CMC and carbopol 934 were selected as polymers.
- The drug and excipient compatibility was studied by using FTIR
- Nine formulations of gels were prepared by taking different quantities of polymers
- The prepared gel was subjected to various evaluation tests like pH, Spreadability, viscosity,

content uniformity and diffusion studies conducted upto 12 hrs.

- All the results were within the limits; by diffusion studies it was observed that formulation F7 shown maximum drug release of 95.49% which was considered as optimized formulation.

ACKNOWLEDGEMENT

The Authors are thankful to Sura Labs, Dilshukhnagar, Hyderabad for providing the necessary facilities for the research work.

REFERENCES

1. Anusha Gundeti, C. Aparna, Dr. Prathima Srinivas Formulation and Evaluation of Transdermal Patch and Gel of Nateglinide IJPPR Research Article September 2015Vol.:4, Issue:2
2. Hindawi Publishing Corporation The Scientific World Journal Volume 2015, Article ID 495271, 7 pages Woo Fong Yen, Mahiran Basri, Mansor Ahmad, and Maznah Ismail
3. Abdullah Mrad, Hind El-Zein and Issa Hassan Preparation and in vitro evaluation of oxybutynin transdermal gel formulations Journal of Chemical and Pharmaceutical Research, 2015, 7(4):1565-1574
4. Diwakar Khadka, Mohammed Gulzar Ahmed, Rajesh Kowti, Pramod Dhakal, AnkitAcharya Formulation And Evaluation Of Transdermal Gel Oflornoxicam And Comparitive Diffusion Study Byiontophoresis And Chemical Enhancers IJAPR /Feb.2015/ Vol. 6/Issue.02 / 40 – 49
5. Sheela A Yadav, Sushilkumar S Poddar Formulation, In-Vitro And In-Vivo Evaluation Of Nanoemulsion Gel For Transdermal Drug Delivery Of Nimodipine
6. Dey S, Mazumdar B, Banwait H, formulation and evaluation of topical gel of aceclofenacgel using different gelling agent. International Journal of Drug Delivery and Research, 2011,3: 156-164.
7. Mr. Hiren Patel, Ms. Mital S. Panchal, Mr. Suresh Shah , Dr. K.R.Vadalia Formulation and Evaluation of Transdermal Gel of Sildenafil Citrate International Journal of Pharmaceutical Research & Allied Sciences Volume 1, issue 3 (2012), 103-118
8. Swati Jagdale, Saylee Pawar Gellified Emulsion of Ofloxacin for Transdermal Drug Delivery System Advanced Pharmaceutical Bulletin, 2017, 7(2), 229-239
9. Enkelejda Goci , Entela Haloci, Skerdilaid Xhulaj, Ledjan Malaj Formulation And In Vitro Evaluation Of Diclofenac Sodium Gel Int J Pharm Pharm Sci, Vol 6, Issue 6, 259- 261
10. Rabinarayan Parhi, Bhaskara Rao Terapalli , B. B. Teja Formulation and In Vitro Evaluation of Minoxidil Topical Gel
11. Asif Nawaz, Syed Umer Jan , Nauman Rahim Khan , Abid Hussain and Gul Majid Khan Formulation and in vitro evaluation of clotrimazole gel containing almond oil and Tween 80 as penetration enhancer for topical application Pak. J. Pharm. Sci., Vol.26, No.3, May2013, pp.617-622
12. Harrison T R., Harrison's Principles of Internal Medicine, 16th Edn, McGraw HillPublishing Company; 1976; 271-274.
13. Metz, M. E., Pryor, J. L., Nesvacil, L. J., Abuzzahab, F., and Koznar, J., "Prematureejaculation: A Psychophysiological review." J. Sex Marital Therapy. 1997, 10, 23-30.

a. Chien, Y. W., Novel Drug Delivery systems. 2 nd Edn, Marcel Dekker Inc. New York:1992; 499.

14. Jain, N. K, Controlled and Novel drug delivery system. 1st Edn, CBS Publications, NewDelhi: 1997; 110-115
15. Ryan, D. G. and Peterson, T. A., "Myths about transdermal drug delivery." Drug Del.Tech. 2003, 3(4), 1-7.
16. Vivek kumar , R., "Formulation and evaluation of MIMOSA PUDICA GEL" Int. J. Pharmacy and Pharm. Sci. 2011, 3(1), 2011, 55-57.
17. Wade, A. and Paul, J. W., Hand Book of Pharmaceutical Excipients. 2nd edition. The Pharmaceutical Press and the American Pharmacists Association, New York, 1994.

a. Kaplan, H. S., "The New Sex Therapy: Active Treatment of Sexual Dysfunctions." Brunner/Maazel, New York, 1974.

18. Washington, D. C., Diagnostic and Statistical Manual of Mental Disorders, 4th Edn, TextRevision. American Psychiatric Association, 2000.
19. Masters, W. H., Johnson, V. E., "Human Sexual Inadequacy."J. Am. Coll. Cardio. 1970.1011-1014.
20. Halcox, J. P., Nour, K. R., Zalos, G., "The effect of sildenafil on human vascularfunction, platelet activation, and myocardial ischemia." J. Am. Coll. Cardiol. 2002, 40, 1232-1240.

21. Mitra J, Mohammad RR and Hedayte S (2006). Mucoadhesive and drug release properties of benzocaine gel. Iranian J. Pharm. Sci., 2: 185-194.
22. Manivannan Rangasamy, Venkata Krishna Reddy Palnati, Lakshmi Narayana Rao Bandaru Formulation development and evaluation of voriconazole sustained release tablets International Current Pharmaceutical Journal, September 2013, 2(10): 165-169
23. Michniak B, Player MR, Chapman J and Sowell JW (1993). In vitro evaluation of a seriesof azone analogs as dermal penetration enhancers. Int. J. Pharm. 91: 85- 93.
24. Aejaz A, Azmail K, Sanaullah S, Mohsin AA. Formulation and in vitro evaluation of aceclofenac solid dispersion incorporated gels. International Journal of Applied Pharmaceutics 2010;2(1 SRC GoogleScholar):7-12.
a. Nayak P, Kumar R. Retromastoid-sub occipital: A novel approach to cerebello pontine angle in acoustic neuroma surgery-our experience in 21 cases. Journal of neurosciences in rural practice 2011;2(1):23-6.
25. Fang J-Y, Huang Y-B, Lin H-H, Tsai Y-H, Transdermal iontophoresis of sodium nonivamide acetate. IV. Effect of polymer formulations, Int J Pharm 173,127–140, 1998.
26. Shin S-C, Lee J-W, Yang K-H, Lee CH, Preparation and evaluation of bioadhesive benzocaine gels for enhanced local anesthetic effects, Int J Pharm 260, 77–81, 2003.
a. Shin S-C, Cho C-W, Enhanced Transdermal Delivery of Pranoprofen from the Bioadhesive Gels, Arch Pharm Res 29, 928-933, 2006.
b. Shina S-C, Chob C-W, Yang K-H, Development of lidocaine gels for enhanced local anesthetic action, Int J Pharm 287, 73– 78, 2004.
27. Hascicek C, Bediz-Olcer A, Gonul N, Preparation and evaluation of different gel formulations for transdermal delivery of meloxicam, Turk J Pharm 6, 177-186, 2009.
a. Singh S, Parhi R, Garg A, Formulation of Topical Bioadhesive Gel of AceclofenacUsing 3-Level Factorial Design, Iranian J Pharm Res 10, 435-445, 2011.
28. Trommer H, Neubert RH. Overcoming the stratum corneum: The modulation of skin penetration. A review. Skin Pharmacol Physiol 2006;19(2):106-21. doi: 10.1159/000091978
29. Jhawat VC, Saini V,Kambooj S, Maggon N. Transdermal drug delivery systems: approaches and advancements in drug absorption through skin. Int J Pharm Sci Rev Res 2013;20(1):47-56.