Formulation and optimization of Novel Extended Release Mucoadhesive Buccal Patches of Carvedilol

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ABSTRACT

The aim of this project work is to development of novel Mucoadhesive formulation for buccal disorders which shows an intensive potential for site specific and sustained release drug delivery system. The Carvedilol was observed physical properties, solubility in different solvents, melting point and partition coefficient. UV spectrogram of Carvedilol scanned from 200- 400 nm, λmax found at 241nm**.** The calibration curve for Carvedilol was prepared in 6.8 pH. FT-IR study was performed to identified drug-excipient interaction. Total five formulation (F-1 to F-5) were prepared using different ratio of Chitosen and Pectin. All the formulated buccal patches were evaluated and found, all are flexible smooth and semi-transparent, weight variation was under limits, average thickness was 0.23mm found, folding endurance between 173-211. All the formulated buccal patches were also evaluated and found, average tensile strength was 0.9 Kg/cm^2 found, drug content was between 0.792 - 0.882 mg/cm^2, percentage moisture content (2.71 – 3.55%), percentage moisture uptake (4.14 – 5.17) and percentage permeation (78.12 – 92.53) also evaluated. All the formulated buccal patches were evaluated for their *In-Vitro* Release. The dissolution study of all formulation shows the percentage drug release were found F1- 55.34%, F2 – 65.43%, F3- 69.52%, F4- 90.32%, and F5- 69.05% in 18 Hour. According to drug release studied **F-4** formulations shows excellent drug release profile in steady way. Kinetic modeling of release profile of F-4 had done. From the data of drug release, it was found that the formulation F-4 follow Zero order and diffusion mechanism for the drug (Carvedilol) release**.** It was concluded that Mucoadhesive patches of Carvedilol were offers enhanced solubility and continuous release of the medicament and bioavailability of the drug and subsequent efficacy is improved.

KEYWORD: Mucoadhesive, Carvedilol, buccal disorders, Extended Release, Buccal Patches

INTRODUCTION

Mucous membrane is the main administration site for bioadhesive systems, although the need for new bioadhesive formulations for dermal administration has also been reported when prolonged cutaneous action is desired[1]. A prolonged effect upon the dermal administration of creams, solutions, and lotions is unexpected, since such preparations can be easily removed from the skin by moisture, temperature and physical movements[2]. Mucoadhesivedrug delivery system through Buccal, sublingual, rectal and nasal mucosa can be faster and systemic mode of non-invasive drug administration to bypass first pass metabolism. Faster delivery and enhanced bio availability of drugs is observed through mucoadhesive administration[3]. The Buccal cavity has wide varieties of functions and it acts as an excellent site for the absorption of drugs which provides a direct entry of such agent in to the systemic circulation; there by avoiding the first pass metabolism and gastrointestinal degradation[4]. However the Buccal route of drug delivery has received much more attention because of its unique advantages over other transmucosal routes[5]. Various adhesive mucosal dosage forms have been developed which include adhesive tablets, gels, ointments, Buccal films and more recently Buccal patches[6].

The aim of this project work is to development of novel Mucoadhesive formulation for buccal disorders which shows an intensive potential for site specific and sustained release drug delivery system. The distinctive advantage of these prepared formulations will be avoiding the initial burst activity, first pass metabolism and gastrointestinal degradation[7]. This formulation will be useful for extended release drug delivery systems for oral cavity disorders[8]. Mucoadhesive buccal patches helps to increase the bioavailability and potency of by using permeation enhancer and formulation optimization[9]. By using polymers will increase the retention time of release of drug in muccal area and prolong the drug delivery of drug which will reduce dose frequency and side effectv[10]. So new extended release Mucoadhesive buccal patches will come in the market which have good bioavailability with less or no side effect.

MATERIAL AND METHOD

API Carvedilol was obtained from Ranbaxy, Devas as gift. Chitosan and Pectin were purchased from Sulab, Varodara. Poly vinyl pyrrolidone (PVP K-30), Glacial acetic acid and Glycerol were purchase d from Rankem, Mumbai. Remaining all reagents used were belongs to L.R. grade.

Preformulation Studies: In the contest of preformulation studies organoleptic properties, solubility, partition co-efficient, melting point and ultraviolet absorption maxima (λmax) were determination. Calibration curve of carvedilol was prepared and physical and chemical drug-excipient compatibility was observed.

Method of Preparation of Mucoadhesive buccal patches: Buccoadhesive patches containing varying amounts of chitosan and pectin were prepared by solvent casting method with slight modification. Chitosan and drug were dissolved in 2% v/v glacial acetic acid solution and pectin was dissolved separately in distilled water. Chitosan solution containing drug was added to pectin solution with stirring. Glycerol 5% v/v was added as plasticizer under constant stirring. To improve patch performance and release characteristics, a water soluble hydrophilic additive, 1% w/v PVP K-30 was added. The resulting viscous solution was casted into petridish and dried in an oven at $50^{O}C$ for 48 hours. The dried films were carefully removed and checked for any imperfection or air bubbles. The patches were packed in an aluminium foil and stored in an air tight glass container to maintain the integrity and elasticity of the patches.

Evaluations of Mucoadhesive buccal patches

Mucoadhesive buccal patches were evaluated by visual observation, physical stability of buccal patches, physical stability of buccal patches, tensile strength, folding endurance, drug content, percentage moisture content, *In-vitro* swelling studies, *In-vitro* Drug Release Studies, and *In-vitro* permeation study.

Kinetic modeling of dissolution data

Drug release kinetics were analyzed by various mathematical models such as a zero-order and first-order kinetic models; Higuchi and Korsmeyer–Peppas models to ascertain the kinetics of drug release**.**

RESULT AND DISCUSSION

Preformulation studies: The Carvedilol was found as white, odorless, tasteless, amorphous powder, freely soluble in methanol, soluble in buffer (pH 6.8) and Ethanol, slightly soluble in 0.1N NaOH and insoluble in 0.1N HCl and water, had melting point 117-118^{O}C and having Partition Coefficient found 8.764. UV spectrogram of Carvedilol scanned from 200- 400 nm,

λmax found at **241nm.** The calibration curve for Carvedilol was prepared in 6.8 pH buffer in the concentration range of 2-10 µg/ml and R^2 value 0.999 also calculated Linear equation (y = 0.040x + 0.000). FT-IR study indicated on the basis of peaks of Carvedilol (pure) and Carvedilol + excipients (Chitosen + Pectin + Glycerol + PVP), that there is no drug-excipient interaction was identified Clark's analysis.

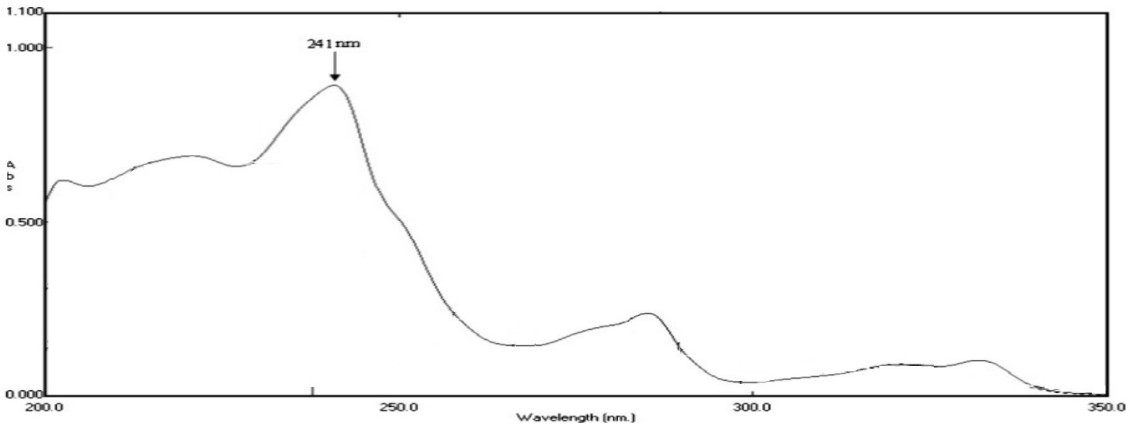

Figure 1: UV spectrogram of Carvedilol from 200- 400 nm

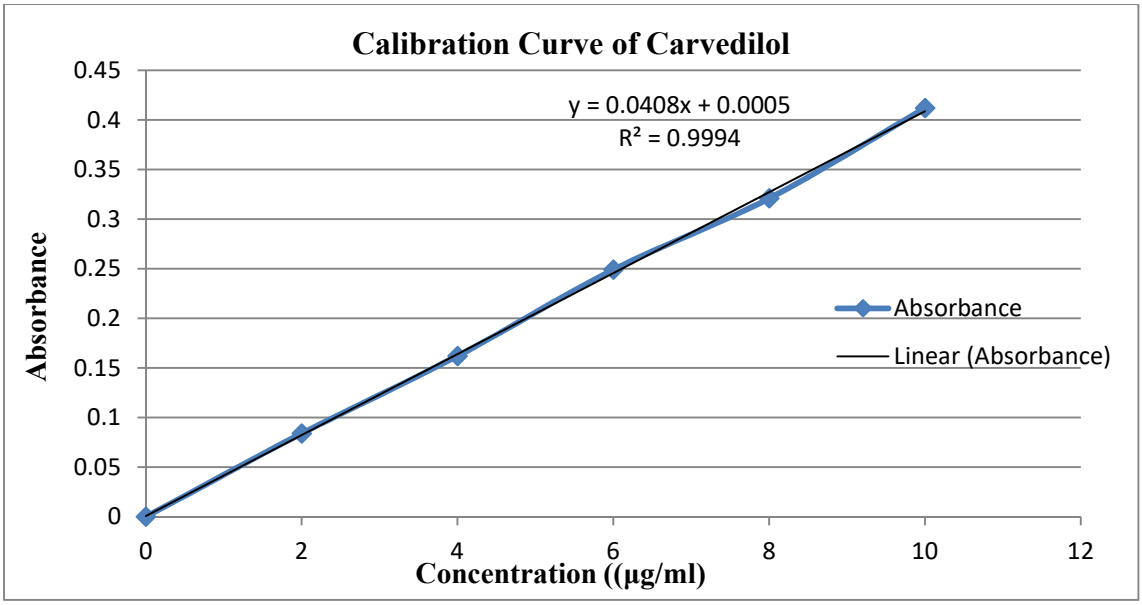

Figure 2: Calibration curve of Carvedilol in phosphate buffer pH 6.8

Drug excipient compatibility study: FT-IR study indicated on the basis of peaks of Carvedilol (pure) and Carvedilol + excipients (Chitosen + Pectin + Glycerol + PVP), that there is no drug-excipient interaction was identified Clark's analysis.

Formulation of Mucoadhesive buccal patches

Table No. 10: Formulation of Mucoadhesive buccal patches

Ingredients	F-1	F-2	F-3	F-4	F-5
Carvedilol (mg)	10	10	10	10	10
Chitosen (mg)	25	33	50	66	75
Pectin	75	66	50	33	25
Ratio of Chitosen: Pectin	1:3	1:2	1:1	2:1	3:1
Glycerol (5%)	5	5	5	5	5
PVP (1%)	1	1	1	1	1

Evaluations of Mucoadhesive buccal patches:

All the formulated buccal patches were evaluated and found, all are flexible smooth and semi-transparent, weight variation was under limits, average thickness was 0.23mm found, folding endurance between 173-211,

Table No. 11: Common parameters of evaluation of buccal patches of Carvedilol

Batch Code	Visual Observation	Weight (g/cm^2)	Thickness (mm)	Folding Endurance
F-1	Semi-Transparent flexible, smooth	0.320 ± 0.11	0.226 ± 0.10	182
F-2	Semi-Transparent flexible, smooth	0.360 ± 0.12	0.234 ± 0.13	173
F-3	Semi-Transparent flexible, smooth	0.333 ± 0.19	0.230 ± 0.16	194
F-4	Semi-Transparent flexible, smooth	0.314 ± 0.20	0.215 ± 0.48	211
F-5	Semi-Transparent flexible, smooth	0.388 ± 0.11	0.267 ± 0.15	192

All the formulated buccal patches were also evaluated and found, average tensile strength was 0.9 Kg/cm^2 found, drug content was between 0.792 - 0.882 mg/cm^2, percentage moisture content

(2.71 – 3.55%), percentage moisture uptake (4.14 – 5.17) and percentage permeation (78.12 – 92.53) also evaluated.

Table No. 12: Evaluation of buccal patches of Carvedilol

Batch Code	Drug content (mg/cm^2)	Tensile strengths (Kg/cm^2)	Moisture uptake (%)	Moisture content (%)	% Permeation
F-1	0.882	0.942	4.35 ± 0.11	2.71± 0.43	78.12
F-2	0.792	0.965	5.17 ± 0.24	3.00 ± 0.34	82.53
F-3	0.801	0.931	4.70 ± 0.19	3.09 ± 0.53	83.27
F-4	0.828	0.967	4.14 ± 0.51	3.55 ± 0.35	92.53
F-5	0.852	0.982	4.65 ± 0.22	3.24 ± 0.62	88.48

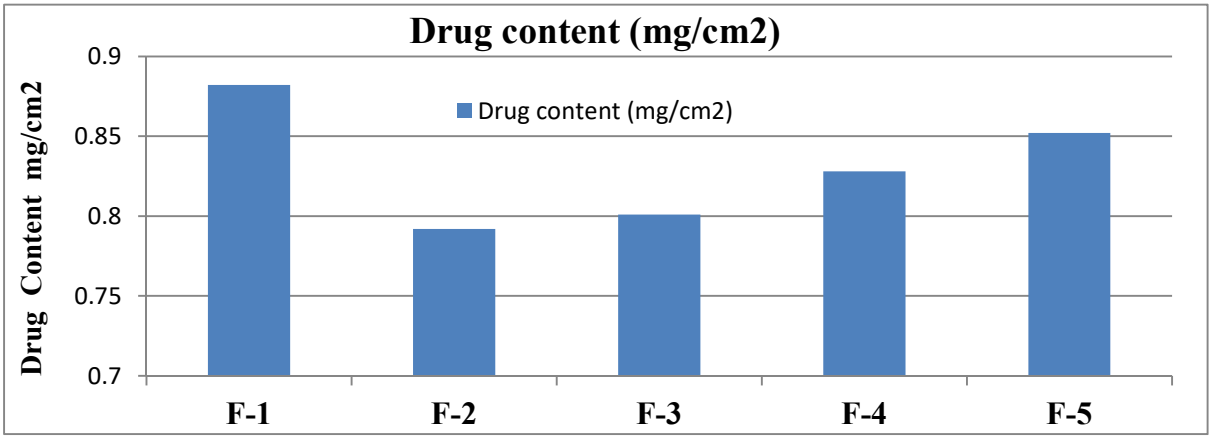

Figure 5: Drug Content of buccal patches of Carvedilol

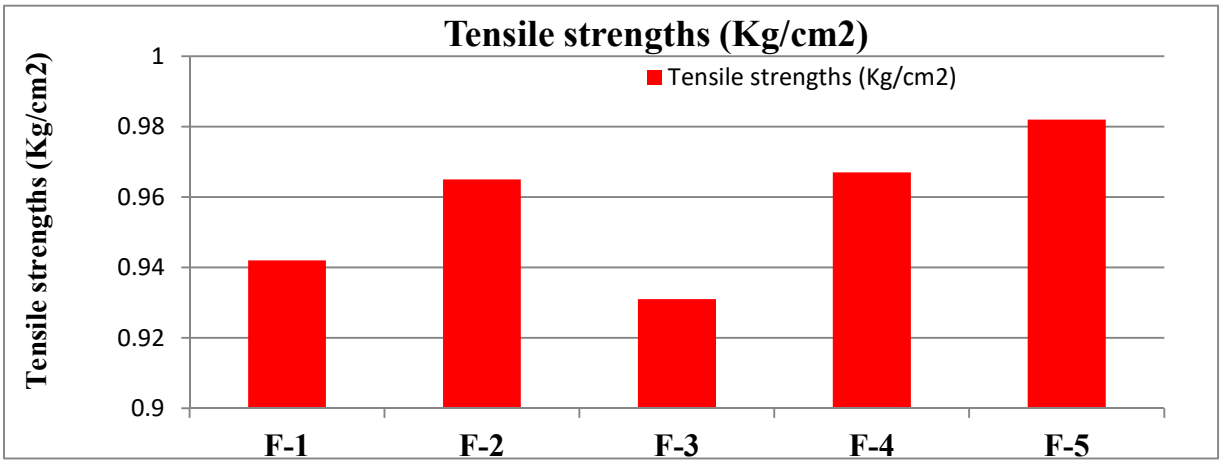

Figure 6: Tennsile Strenths of buccal patches of Carvedilol

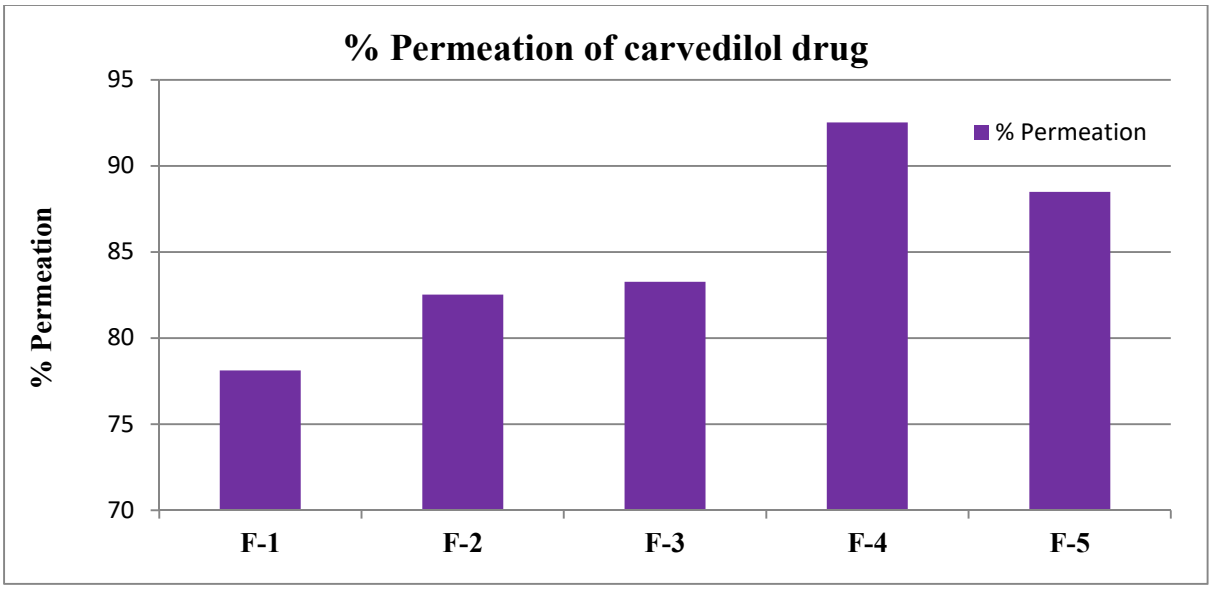

Figure 7: % Permeation of buccal patches of Carvedilol

***In-Vitro* Drug Release studies**

All the formulated buccal patches were evaluated for their *In-Vitro* Release. The dissolution study of all formulation shows the percentage drug release were found F1- 55.34%, F2 – 65.43%, F3- 69.52%, F4- 90.32%, and F5- 69.05% in 18 Hour. According to drug release studied **F-4** formulations shows excellent drug release profile in steady way.

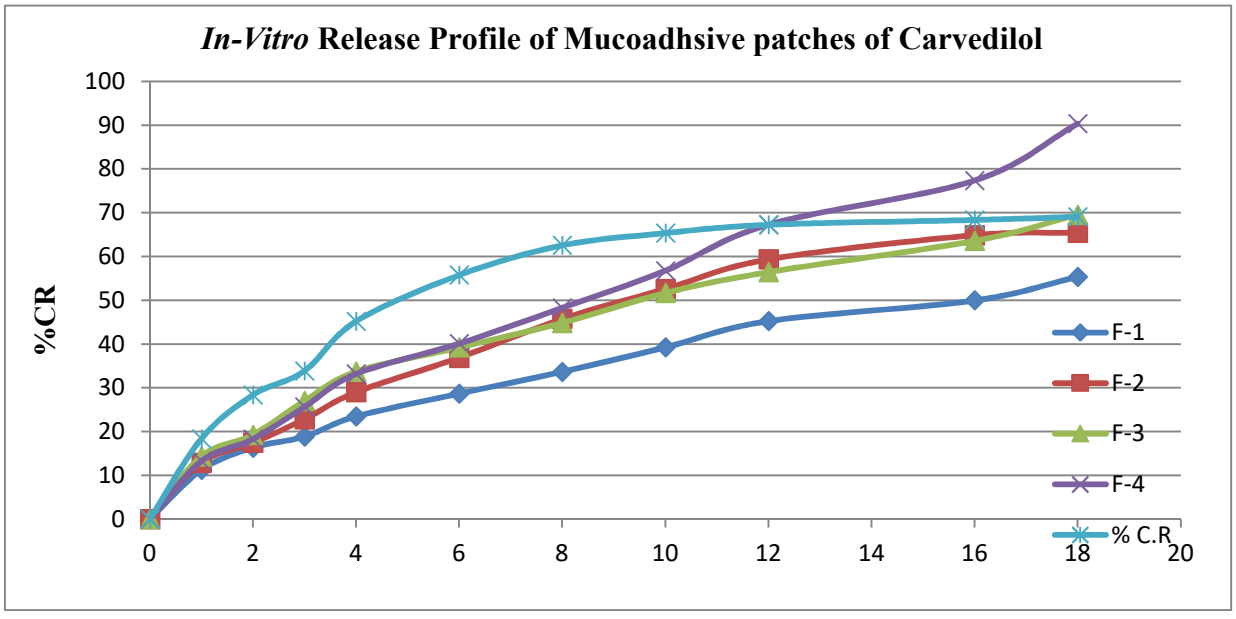

Figure 8: *In-Vitro* Release Profile of Mucoadhsive patch of Carvedilol

Drug release kinetics models of Mucoadhesive patches

Kinetic modeling of release profile of F-4 had done. From the data of drug release, it was found that the formulation F-4 follow Zero order and diffusion mechanism for the drug (Carvedilol) release.

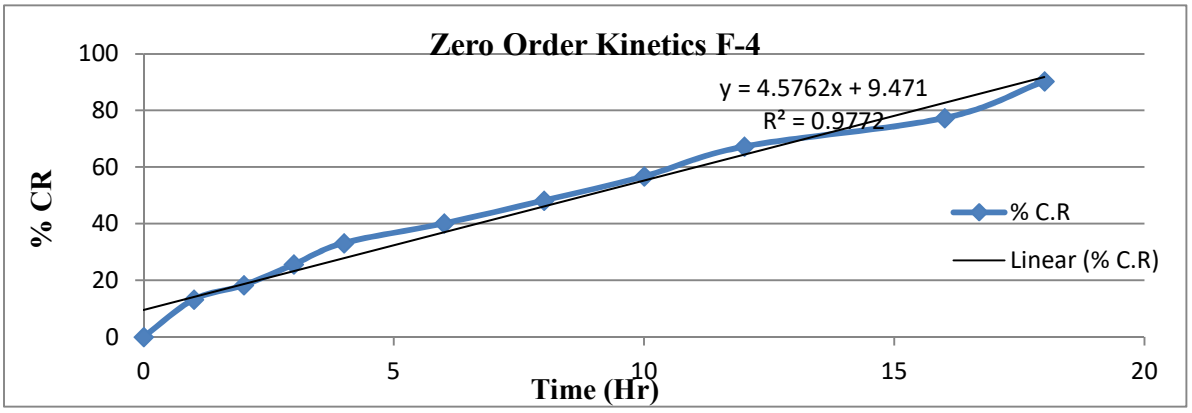

Figure 9: Zero Order Kinetics of Mucoadhesive patches of Cavedilol

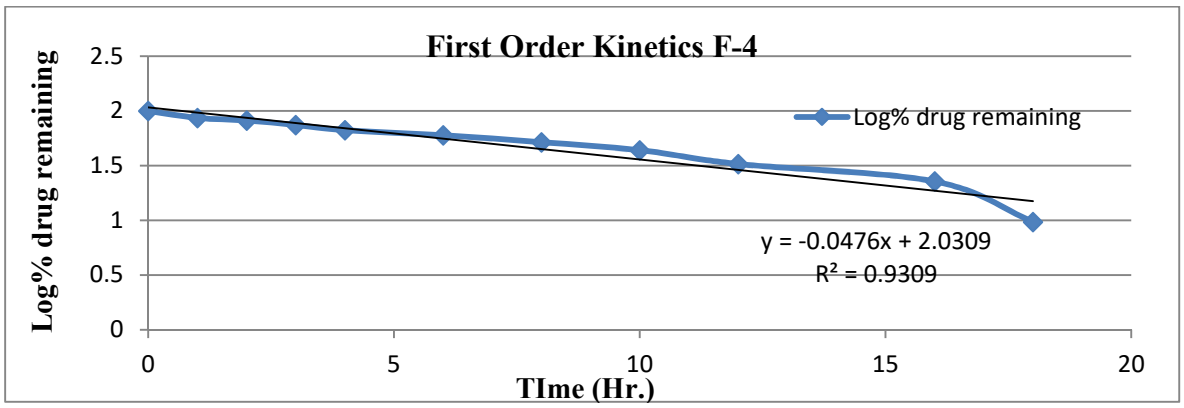

Figure 10: First order Kinetics of Mucoadhesive patches of Cavedilol

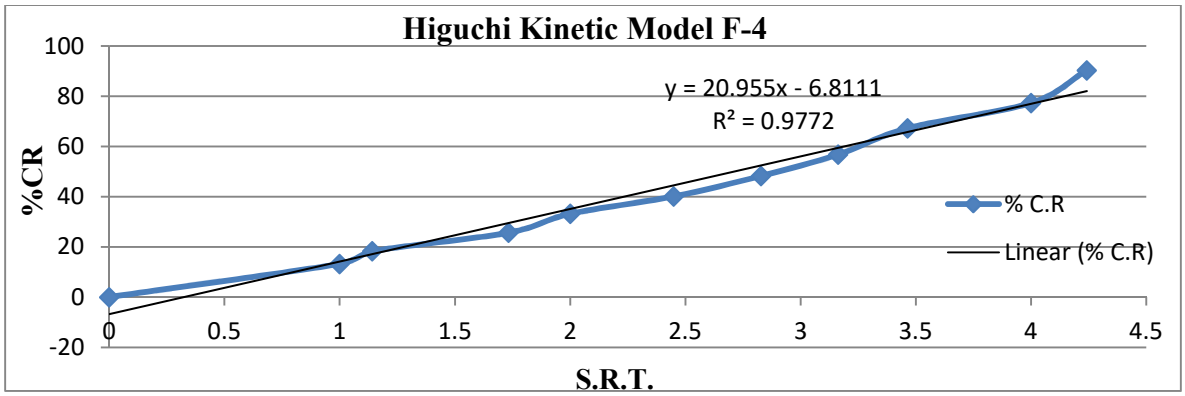

Figure 11: *Higuchi* Kinetic model of Mucoadhesive patches of Cavedilol

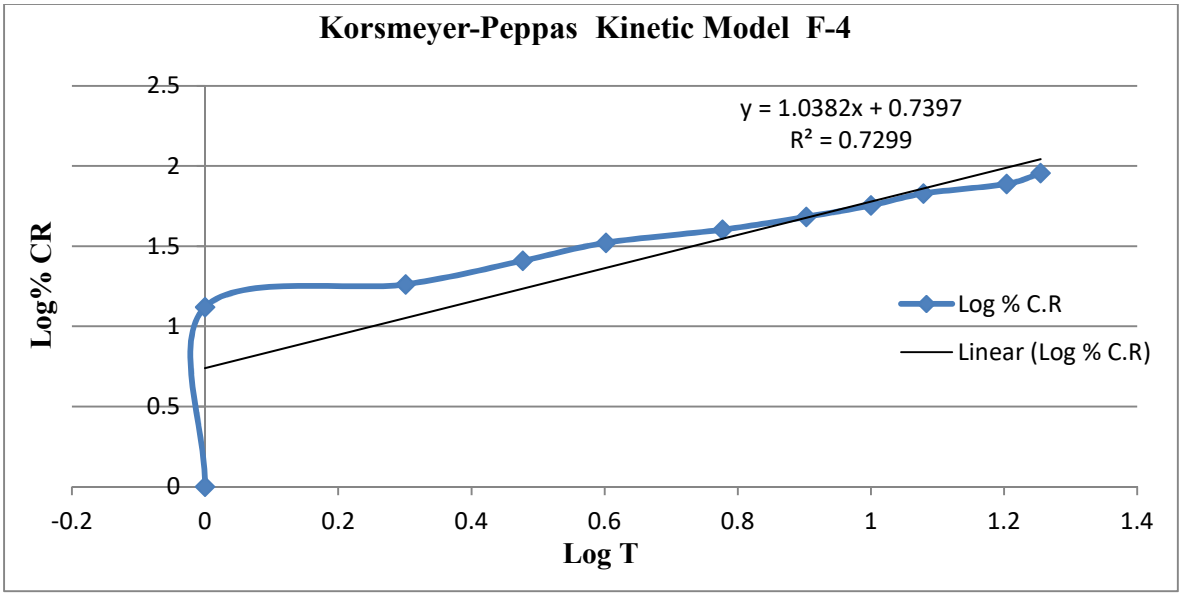

Figure 12: Korsmeyer-Peppas plots of Mucoadhesive patches of Cavedilol

CONCLUSION

Mucoadhesive patches containing varying amounts of chitosan and pectin were prepared by solvent casting method with slight modification. Glycerol 5% was added as humectants and PVP 1% plasticizer was added under constant stirring. Because Caredilol is insoluble in water so, the drug requires a novel drug delivery system which can provide enhanced solubility, an extended period of time and improve absorption via skin. Buccoadhesive patches were characterized for compatibility study, particle size and shape, % entrapment, *in-vitro* drug release. Due to excipients matrix character, these drug delivery systems showed good enhanced solubility and Controlled release, required for bioavailability and therapeutic activity. Carvedilol induced irritation on skin due to high dose can also be reduced by slow release of drug. Major advantages of this delivery system include ease of preparation, good enhanced solubility, high % Drug content and controlled drug release. From this study, it was concluded that Mucoadhesive patches of Carvedilol were offers enhanced solubility and continuous release of the medicament and bioavailability of the drug and subsequent efficacy is improved.

CONFLICT OF INTEREST

There are no conflicts of interests

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