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Formulation and evaluation of doxepin hydrochloride by fast dissolving buccal film

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Abstract

Tricyclic antidepressants, as doxepin hydrochloride (DH), may also have analgesic neighborhood effect due to its biochemical mechanism of action. This is commonly performed via drug to be administers directly into the blood flow via the Buccal mucosa through using fast dissolving movie system. The main aim of the study was to formulate and evaluate Doxepin hydrochloride by fast dissolving buccal film. The Doxepin hydrochloride buccal film were prepared by the solvent casting method by using the different polymers (HPMC E15, PVA, and HEC). The FTIR test is conducted by this test there was no interaction between the drug and polymers. Then buccal film were evaluated for weight uniformity, thickness uniformity, folding endurance, disintegration study, drug content uniformity, and invitro drug release. The weight uniformity ranged from 47.00 to 55.33mg, thickness ranged from 0.17 to 0.25nm, folding endurance ranged from 344 to 355mm drug content ranged from 84 to 98% and disintegration study ranged from 42.0 to 54.3. The F9 formulation showed highest drug release i.e., 99.96% within 4 minutes. The IR spectra showed stable properties of doxepin hcl mixture of polymers used and revealed the absence of interaction between drug and selected polymer, stability studies were as per ich guideline and result indicated that the selected formulation was stable.

Keywords: Doxepin hydrochloride; Buccal film; FTIR; *In-vitro* Drug release

1. Introduction

In gastrointestinal drug delivery the drug to be administered within the shape of pill, drug to be input in to the systemic movement it could require extra time it now not give a fast onset of action and to undergo rapid skip metabolism big quantity of drug to be loosed. Drug to be administered in intravenous it isn't always self-administered route [1].

Drug absorption throughout the oral mucosa, two essential routes of absorption is involved in oral mucosal drug permeation the Trans cellular or intracellular direction (in which pills permeate immediately through the cells) and the Para cellular or intercellular direction (where drugs permeate via passive diffusion through the areas between the cellular) [2].

Doxepin is a medication used in the treatment of predominant depressive disease, tension, insomnia, as well as within the control of pores and skin pruritus. It is in the tricyclic antidepressant class of medications [3].

It belongs to BCS class-I, the significance of using a tream-based approach to control sufferers with principal depressive disorder [4].

The shipping device is simply placed on a affected person's tongue or any oral mucosal The delivery system is clearly located on a affected person's tongue or any oral mucosal tissue. Instantly moist through saliva because of presence of hydrophilic polymer and other excipients, the Strips rapidly hydrates and dissolves to release the drugs for oral mucosal

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absorption.The tissue of the oral mucosa consists of a multilayered epithelium covered with mucus, together with a stratum duodenum, stratum filament to sum, stratum supra basale and stratum basale. Below this, lies a basal lamina. The basal lamina connects the epithelium to a connective tissue layer, the lamina propria. Below lamina propria is the sub mucosa.

Epithelium serves because the mechanical barrier that protects the underlying tissues while lamina propria acts as a mechanical help and additionally incorporates blood vessels and nerves [5].

The ease of accessibility referred to above approach oral mucosal drug transport structures are easy to administer.(i) Buccal transport: is drug management through the mucosal membranes lining the cheeks and the vicinity among the gums and upper and decrease lips to the systemic stream. (ii)Sublingual delivery: is systemic transport of drugs through the mucosal membranes lining the ground of the mouth to the systemic flow [6].

However, the worry of taking solid tablets and the danger of choking for sure patient populace still exist regardless of their brief dissolution/disintegration time. Recent development in novel drug shipping device goals to beautify protection and efficacy of drug molecules by formulating a handy dosage form for administration. One such technique is rapidly dissolving Strips. It includes a very thin oral strip, which releases the lively aspect right away after uptake into the oral cavity. Rapid Strips combines all of the advantages of tablets (precise dosage, smooth software) [7].Advantages of rapid dissolving film Improved oral bioavailability of drug as hepatic first pass impact is reduced.(i)Fast onset of movement as drug enters without delay within the systemic circulate.(ii)No worry of obstruction or chocking.(iii)No want of water during Strips administration.(iv)Reduction in dose of the drug.(v)Taste covering.(vi)Improved patient compliance.(vii)Enhanced balance [8].Dissadvantages of fast dissolving film (i)Drugs whose healing dose is more than 40mg can't be included in the Strips.(ii)Challenge of keeping dose uniformity in Strips [9].

2. Material and methods

Doxepin hydrochloride was purchased from balaji Chemicals. Hydroxypropyl methylcellulose (HPMC E 15), polyvinyl alcohol (PVA), Hydroxyethylcellulose (HEC), from SD fine chem limited. All the reagents were analytical grade.

2.1. Determination of λ max of Doxepin hydrochloride in using phosphate buffer pH 6.8

Accurately weighed accurately weighed quantity of 100 mg of Doxepin hydrochloride was taken in 100 ml volumetric flask and made up to 100 ml using phosphate buffer of pH 6.8

2.1.1. Scanning

From the above stock solution, 80 µg/ml solution was prepared and scanned between 200-400nm by keeping methanol as blank. The absorption maxima of 292 nm for DOXEPIN HYDROCHLORIDE was obtained and used for further studies.

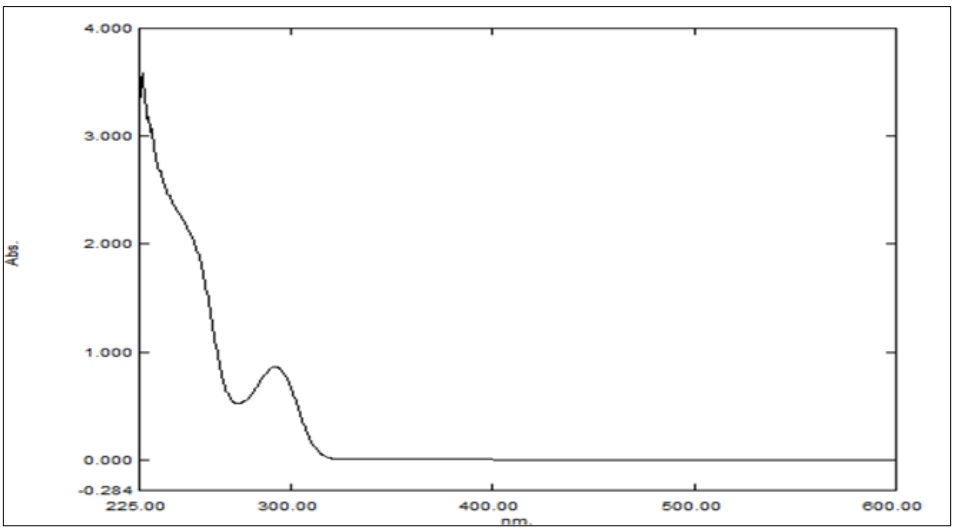

Figure 1 Determination of λ max of Doxepin hydrochloride in using phosphate buffer pH 6.8

2.2. Fourier-transform infrared spectroscopy (FT-IR)

There is usually a possibility of drug-excipients interaction in any system due to their intimate touch. The method hired on this look at to understand drug- excipients interactions is IR spectroscopy. IR spectroscopy is one of the most effective analytical strategies which offer the opportunity of chemical identification. Infra-purple spectra of pure drug DM and formulations were scanned through using FTIR technique.

2.3. Preparation of calibration curve in phosphate buffer of pH 6.8

The standard solution of doxepin hydrochloride was prepared using, 100 mg of doxepin hydrochloride was dissolved in 100 mL volumetric flask of simulated saliva buffer 6.8 (pH) to give a concentration of 1000 mg/ml. The prepared standard solution was pipetted out in different volume of 10, 20, 30, 40, 50, 60, 70, 80 ml was pipette out in a 10 ml volumetric flask and finally diluted up to the mark with simulated saliva buffer. The aliquots were analysed at 292 nm. The plot of concentration v/s absorbance, was plotted.

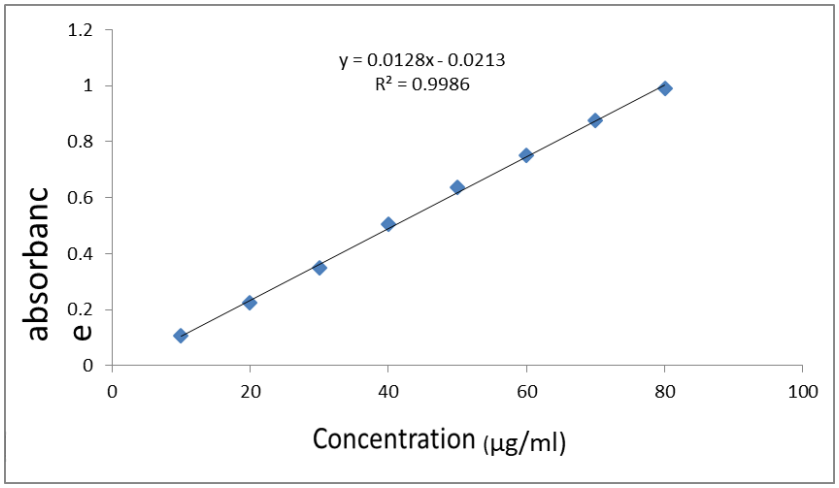

Figure 2 The Standard graph of Doxepin hydrochloride in phosphate buffer pH6.8

2.4. Formulation design

2.4.1. Formulation of fast dissolving buccal film

Table 1 Composition of different formulation of Doxepin hydrochloroide fast dissolving buccal film

Formulation code	Polymer and its compostion (mg)				Plasticizer glycol (ml)	Sodium Saccharin (mg)	Vanillin (mg)	D.Water (ml)
	Drug	HPMC E15	HEC	PVA				
F1	120	300	---	---	0.1	2	2	10
F2	120	350	---	---	0.1	2	2	10
F3	120	400	---	---	0.1	2	2	10
F4	120	---	300	---	0.1	2	2	10
F5	120	---	350	---	0.1	2	2	10
F6	120	---	400	---	0.1	2	2	10
F7	120	---	---	300	0.1	2	2	10
F8	120	---	---	350	0.1	2	2	10
F9	120	---	---	400	0.1	2	2	10

From the preliminary physical observation of the strips prepared the best compositions were used for the incorporation of Doxepin hydrochloride solvent casting. Doxepin hydrochloride 120mg was dissolved in the polymeric solution, then

polymers are added (PVA, HEC, and HPMC E15), propylene glycol (plasticizer) was added and stirred to form a homogeneous solution. Finally Vanillin and Sodium saccharin are added and stirred to form a homogeneous mixture. The solution was casted in a mould 6×8 cm (length and width). Then kept in hot air oven at 60ºC for 24 hours. The film thus formed was cut into size of 2×2 cm square strips. The prepared square thin orals strips were packed using single pouches, blister card with multiple units, multiple-unit dispenser, and continues roll dispenser aluminum pouch and stored in desiccator.[10]

2.5. Evaluation of Doxepin hydrochloride fast dissolving buccal film

2.5.1. Physical appearance and surface texture of strips

This parameter was checked simply with visual inspection of strips and evaluation of texture.

2.5.2. Weight uniformity of strips

Three strips of the size 2×2 cm were weighed individually using digital balance and the average weights were calculated.

2.5.3. Thickness of strips

Thickness of the strips was measured using screw gauge with a least count of 0.01mm at different spots of the strips. The thickness was measured at three different spots of the strips and average was taken.[11].

2.5.4. Folding endurance of strips

The flexibility of strips can be measured quantitatively in terms of what is known as folding endurance. Folding endurance of the strips was determined by repeatedly folding a small strip of the strips (approximately 2x2 cm) at the same place till it broke. The number of times strips could be folded at the same place, without breaking gives the value of folding endurance.

2.5.5. Drug content uniformity of strips

The strips were tested for drug content uniformity by UV Spectrophotometric method. Strips of 2×2 cm size were cut from three different places from the casted strips. Each film was placed in 100 mL volumetric flask and dissolved in simulated saliva pH 6.8 and 2 mL is taken and diluted with water up to 10 ml. The absorbance of the solution was measured at λ max246 nm using UV/ visible spectrophotometer (Shimadzu, japan). The percentage drug content was determined. [12].

2.5.6. In vitro drug release

The release rate of Doxazosin mesylate fast dissolving oral strips was determined by using the 250 mL beaker placed on magnetic stirrer and adds magnetic beads into the beaker. The RPM of the magnetic bead was maintained at 50 RPM. The film with 2×2 cm was placed in the 100 mL of 6.8 pH simulated saliva as dissolution medium, and temperature was maintained at 37°C. From this dissolution medium, 2 mL of the sample solution was withdrawn at different time intervals. The samples were filtered through Whitman filter paperand absorbance was determined 246nm using double beam UV- Visible spectrophotometer.

2.5.7. Permeation study

The prepared fast dissolving Buccal strips are placed in the Franz diffusion cell on the upper membrane of the (donor compartment) and the receptor compartment contain a simulated saliva (10 ml) it can be contact with the permeation membrane washed and soaked with phosphate buffer 6.8 upper side of the donor compartment contain a film attach the film of length and width (2×2) cm it contains 1 mg of drug. And the receptor compartment it contain a simulated saliva and magnetic bead and this diffusion compartment placed in the magnetic stirrer the drug permeation start through the dialysis membrane and enter in to the receptor compartment the drug to be enter in the receptor compartment and this solution taken 2 ml every 5 minutes up to 45 minutes and maintain the sink condition by replace the 2ml of simulated saliva in to the receptor Compartment and this every interval taken samples analyzed by (Shimadzu) UV-visible spectrophotometer.[13]

3. Results and discussion

3.1. Drugs-polymer interaction study by FT-IR spectrophotometer:

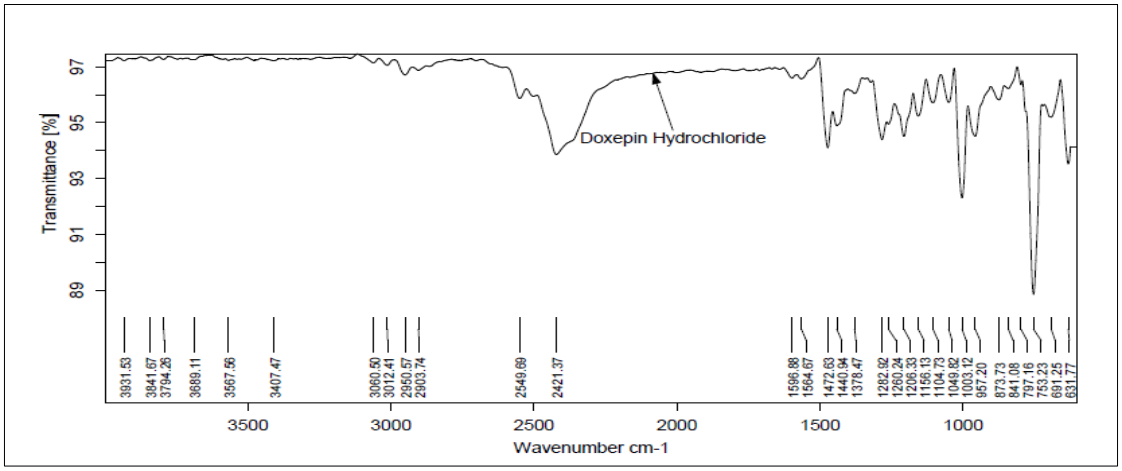

Figure 3 The FTIR spectrum of pure Doxepin hydrochloride

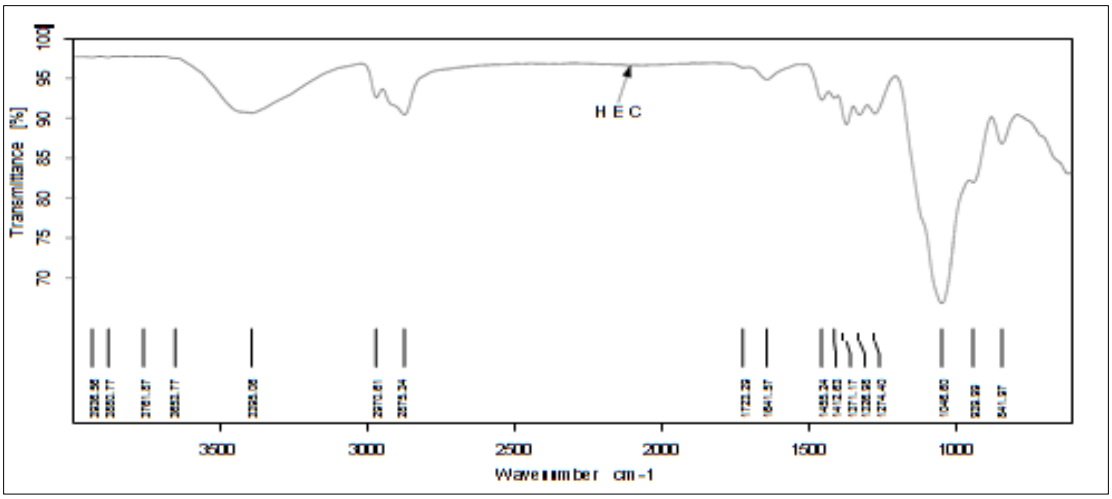

Figure 4 The FTIR Spectrum of drug +HEC

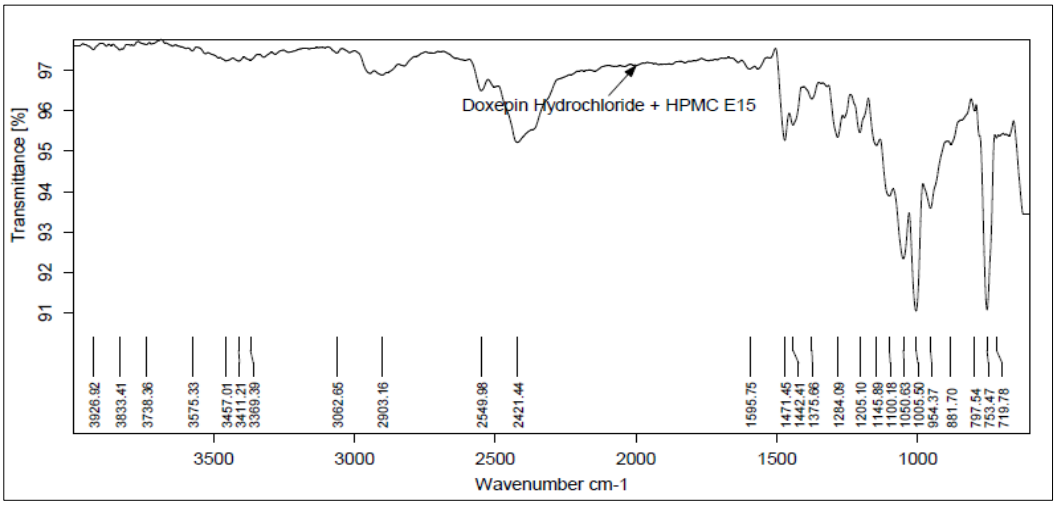

Figure 5 The FTIR Spectrum of Drug+HPMC E15

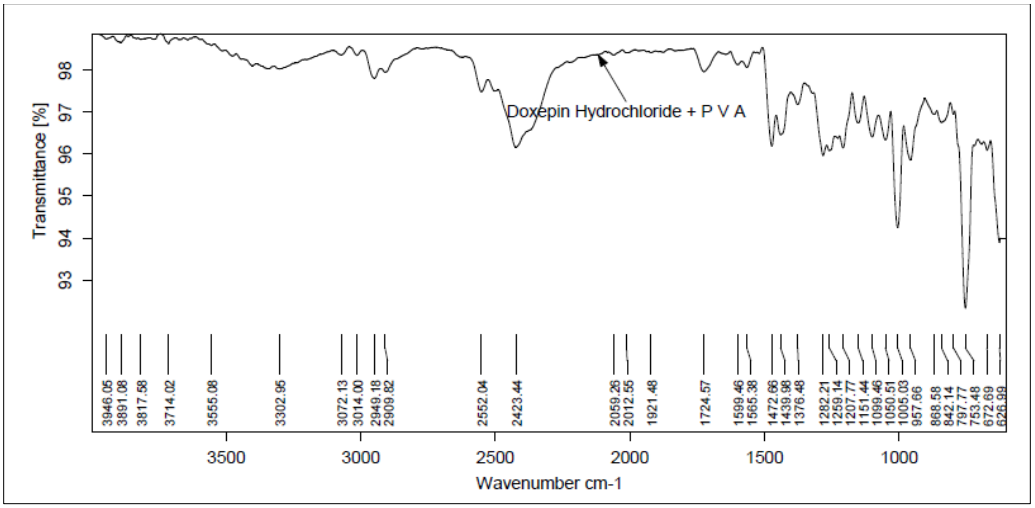

Figure 6 The FTIR Spectrum of Drug+PVA

An FT-IR spectroscopy study has been carried out separately to check the compatibility between the drug (Doxepin hydrochloride) and the polymers (HPMC E15, HEC, PVA) used for the preparation of Drug and polymers. The FT-IR was performed for drug, polymers, and physical mixture of drug and polymers.

Perusal to the above FTIR spectra, the characteristic peaks of Doxepin hydrochloride of pure spectrum was retained in the FTIR spectra of physical mixture of drug with HPMC E15, PVA, HEC. Therefore, there was no drug polymer interaction is found. Hence, these polymers were used for the preparation of Buccal strips.

Table 2 Interpretation of FTIR spectra

SI.NO	Name of the Compound	Wave number (cm^{-1})	Functional group
1	Doxepin hydrochloride	1596.88	C=C stretching
		2903.16	C-H stretching
		1003.12	C-O stretching
2	DM: HEC	1599.66	C=C stretching
		2909.20	C-H stretching
		1006.61	C-O stretching
3	DM: HPMC E15	1595.75	C=C stretching
		2903.16	C-H stretching
		1005.05	C-O stretching
4	DM: PVA	1599.46	C=C stretching
		2909.82	C-H stretching
		1005.03	C-O stretching

3.2. Drug content uniformity of various Doxepin hydrochloride fast dissolving buccal film

The drug contents the Table no.4. The drug content results of buccal film were obtained in the range from 91.0 to 98.0%.

Table 3 Data of drug content of Doxepin hydrochloride fast dissolving buccal film

Formulations Code	Drug Content %
F1	91±0.18
F2	90±0.34
F3	91±0.18
F4	84±0.15
F5	85±0.24
F6	86±0.26
F7	94±0.12
F8	96±0.17
F9	98±0.22

3.3. Release studies

The drug releases from the buccal film were studied by *Franz* diffusion method. The *in vitro* release profiles of Doxepin hydrochloride from Doxepin hydrochloride of buccal film are shown in Table No.5. The cumulative percentage releaseof drug from 82.56 to 99.96% depending upon the drug polymer ratio.

Table 4 Percentage drug released from different formulations (F1-F8) during 12 Hours

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
2	72.53	75.86	85.23	72.53	69.14	78.56	89.96	90.86	90.86
4	74.56	76.96	85.13	74.56	71.68	77.89	90.86	96.79	99.96
6	80.56	83.56	86.88	76.96	70.72	80.63	86.49	89.83	94.32
8	88.86	86.89	88.13	80.56	73.85	84.36	82.67	82.63	86.46
10	83.13	78.26	75.89	88.86	82.56	87.96	77.16	79.91	80.02
12	71.27	73.05	69.42	86.89	75.56	75.23	75.87	73.85	78.25
14	70.23	69.89	65.45	73.05	73.05	73.20	69.83	71.83	71.83
16	65.96	65.45	60.53	69.89	58.28	69.52	71.63	70.72	70.72
18	62.28	60.53	58.28	65.45	56.12	62.40	66.14	69.62	69.62
20	60.44	58.28	56.12	60.53	54.45	60.09	64.29	69.43	69.43

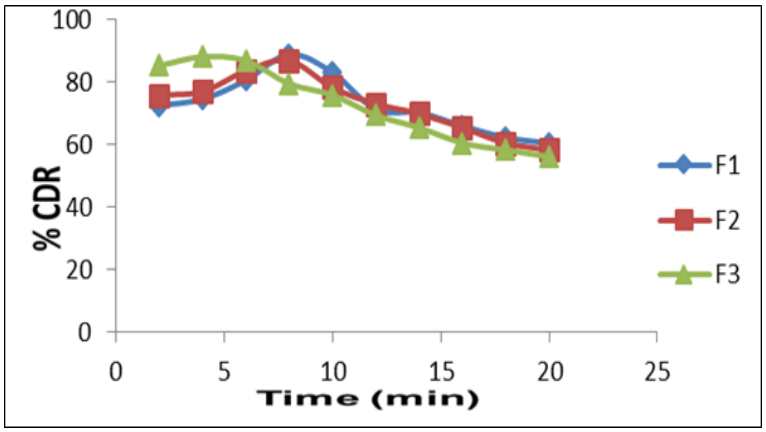

Figure 7 *In-vitro* drug release profile of formulations F1-F3

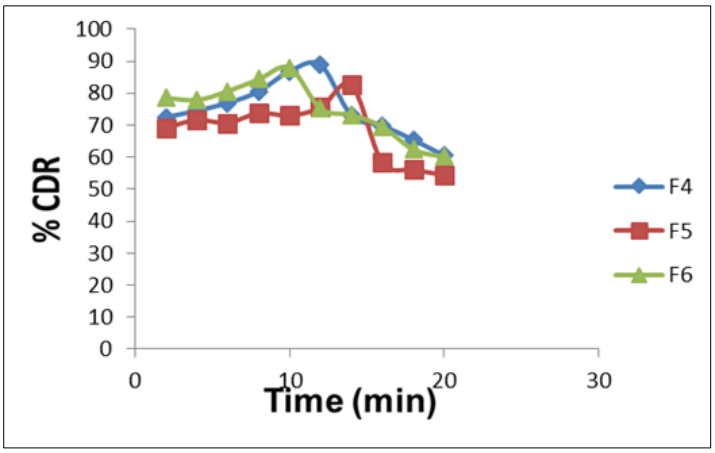

Figure 8 *In-vitro* drug release profile of formulations F4-F6

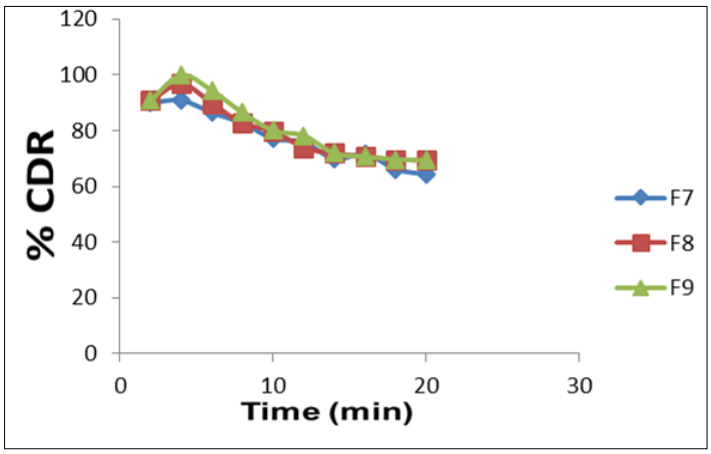

Figure 9 *In-vitro* drug release profile of formulations F7-F9

4. Conclusion

From the present research work that is Formulation and evaluation of Doxepin hydrochloride fast dissolving buccal film polymeric strips were prepared by solvent casting technique using HPMC E15, HEC, PVA, FT-IR studies revealed that there was no interaction between the selected drug and polymers. The all batches F9 was optimized after considering their weight uniformity, thickness of strips, folding endurance and drug content uniformity, disintegration, and invitro drug release profile. And all the formulation showed F6 having polumer concentration PVA showed better drug release 99.96% in 4minutes.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The author have no conflict of interest regarding the work

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