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DESIGN, EVALUATION AND COMPARITIVE STUDIES OF ORAL THIN FILMS AND EDIBLE GEL LOADED WITH ANTI HISTAMINE DRUG FOR GERIATRICS AND PEDIATRICS

Venkata Anupama M*, R. Shireesh Kiran, V. Uma Maheswar Rao

Department of pharmaceutics, CMR College of Pharmacy, Hyderabad, Telangana, India.

ABSTRACT

The Aim of present study is to Design, Evaluate & Compare studies between fast dissolving Oral thin films (OTF) & Edible gel (EG) loaded with Antihistamine drug for Geriatrics and Pediatrics. The Anti-Histamine Drug called Desloratadine is a tricyclic antihistamine, which has a selective and peripheral H1-antagonist action used to treat allergies. Twelve Formulations (F1–F12) of OTF were prepared by casting method using different concentrations of polymers i.e, Sodium alginate (1, 1.5, 2w/v %) and Xanthum (0.4, 0.7w/v %), as the conc. of polymer increased tensile strength and folding endurance were improved with more dissolution time. Ten Formulation (EG1-EG10)of EG were prepared by varying concentrations of Gellan Gum (0.1-0.5%), 0.3% and above concentration of polymer showed good physical and Rheological properties. Optimized Formulation among OTF was F4 with 1.5% Sodium alginate showing good folding endurance, tensile strength, disintegration time and 98.9% drug release with no casting problem and appearance. Optimized formulation among EG was EG8 with no syneresis showing 99% drug release with good consistency and viscosity increasing the mouth feel. Comparative study parameter of F4 and EG8 clearly revealed the instability of OTF and stability of EG at room temperature and also due to its high patient compliance based on appearance and ease of administration, EG was preferred as better dosage form for geriatrics and paediatrics.

Key words: Desloratadine, Edible Gel, OTF, Paediatrics and Geriatrics.

INTRODUCTION

Oral route is most preferred route by medical practitioners and manufacturer due to highest acceptability of patients. About 60% of all dosage forms available are the oral solid dosage form. The lower bioavailability, long onset time and dysphagia patients turned the manufacturer to the parenteral and liquid orals. But the liquid orals (syrup, suspension, emulsion etc) have the problem of accurate dosing mainly and parenteral are painful drug delivery, so most patient incompliance.

Each pharmaceutical company wants to formulate the novel oral dosage form which has the higher bioavailability, quick action and most patient compliance. So they formulate the fast dissolving tablets by using superdisintegrants and hydrophilic ingredients. Fast dissolving drug delivery systems were first developed in the late 1970s as an alternative to conventional dosage forms for Pediatric and Geriatric patients who experience difficulties in swallowing traditional oral solid-dosage forms.

Systemic drug delivery through the sublingual route had emerged from the desire to provide immediate onset of pharmacological effect. Dysphagia (difficulty in swallowing) is a common problem of all age groups, especially elderly, children, and patients who are mentally retarded, uncooperative, nauseated or on reduced liquid intake/diets have difficulties in swallowing these dosage forms [1, 2].

Sublingual administration of the drug means placement of the drug under the tongue and drug reaches directly in to the blood stream through the ventral surface of the tongue and floor of the mouth. The drug solutes are rapidly absorbed into the reticulated vein, which lies underneath the oral mucosa, and transported through the facial veins, internal jugular vein, and brachiocephalic vein and then drained into systemic circulation.

The main mechanism for the absorption of the drug in to oral mucosa is via passive diffusion into the lipoidal membrane [3]. The absorption of the drug through

*Corresponding Author Venkata Anupama M E mail: anupamachowdary11@gmail.com

the sublingual route is 3 to 10 times greater than oral route and is only surpassed by hypodermic injection. For these formulations, the small volume of saliva is usually sufficient to result in tablet disintegration in the oral cavity.

Sublingual absorption is mostly rapid in action, but also short acting in duration. Nitroglycerine, for example, is an effective antianginal drug but is extensively metabolized when taken orally (>90%). It is rapidly absorbed through the sublingual mucosa, and its peak plasma level is reached within 1-2 min. Because of its short biological half-life (3-5 min.), however the blood concentration of nitroglycerine declines rapidly to a level below the therapeutic concentration within 10-15 min.

In terms of permeability, the sublingual area of the oral cavity is more permeable than the buccal (cheek) area, which in turn is more permeable than the palatal (roof of the mouth) area. The differences in permeability are generally based on the relative thickness, the blood supply, and degree of keratinization of these membranes. In addition to the differences in the permeability of the various mucous membranes, the extent of drug delivery is also affected by the physicochemical properties of the drug to be delivered [4].

Sublingual products have been developed for numerous indications ranging from migraines (for which rapid onset of action is important) to mental illness (for which patient compliance is important for treating chronic indications such as depression and schizophrenia) [5].

Oral Thin Films

Fast dissolving oral films (FDOFs) or Oral wafers or Oral strips (OS) or sublingual strips or oral thin films (OTF) are the most advanced form of oral solid dosage form due to more flexibility and comfort. It improves the efficacy of APIs by dissolving within minute in oral cavity after the contact with saliva without chewing and no need of water for administration. It gives quick absorption and instant bioavailability of drugs due to high blood flow and permeability of oral mucosa is 4-1000 times greater than that of skin [6-9]. FDOFs are useful in patients such as pediatric, geriatrics, bedridden, emetic patients, diarrhea, sudden episode of allergic attacks, or coughing for those who have an active life style. It is also useful whether local action desired such as local anesthetic for toothaches, oral ulcers, cold sores or teething. OTFs also have an established shelf life of 2-3years, depending on the API but are extremely sensitive to environmental moisture [10].

The OTFs place as an alternative in the market due to the consumer's preference for a fast-dissolving product over conventional tablets / capsules. The oral thin-film technology is still in the beginning stages and has bright future ahead because it fulfills all the need of patients. Eventually, film formulations having drug/s will be commercially launched using the OTF technology [11].

Oral thin films, a new drug delivery system for the oral delivery of the drugs, were developed based on the technology of the transdermal patch. The delivery system consists of a very thin oral strip, which is simply placed on the patient's tongue or any oral mucosal tissue, instantly wet by saliva the film rapidly hydrates and adheres onto the site of application. It then rapidly disintegrates and dissolves to release the medication for or mucosal absorption or with formula modifications, will maintain the quick-dissolving aspects allow for gastrointestinal absorption to be achieved when swallowed. In contrast to other existing, rapid dissolving dosage forms, which consist of liophylisates, the rapid films can be produced with a manufacturing process that is competitive with the manufacturing costs of conventional tablets.

EDIBLE GEL

Oral administration is the most popular route due to ease of ingestion, pain avoidance, no requirement of sterile conditions, less expensive to manufacture and patient compliance. However, tablets, capsules, and liquids, which are used orally, are difficult to swallow in case of dysphagia patients [3-4]. Patients with advanced age cannot easily take tablets or capsules. The irritation or pain resulting from contact of the solid preparation with the oral cavity or with the larynx and pharynx, or physical injury caused upon rubbing of the solid preparation against mucous membrane can give discomfort to a patient. However, certain modifications are undesirable, such as crushing of the enteric-coated or sustained-release tablet which can lead to adverse events.Crushed tablets are the most frequent cause of obstruction of feeding tubes, which results in increased morbidity, trauma to the patient besides the cost of replacing the tube (surgical). Dysphagia is a clinical syndrome resulting from a biomechanical disorder defined as "an inability to swallow, or a sensation that solids or liquids do not pass easily from the mouth to the stomach". Swallowing disorders (dysphagia) occur in all age groups, preterm babies to the elderly. The problem of swallowing tablets was more evident in geriatric and pediatric patients, as well as travelling patients.

Des loratidine available as tablets and syrups are found difficult for swallowing for dysphagic patients. Injections cause pain at the site of injection and also needs a trained person to administer. Thickened liquids play a vital role in reducing risk of aspiration for dysphagia patients. Previous studies have indicated the importance of viscosity as a bolus variable during the swallowing process. Dietary professionals work closely with the speech-language pathologist (SLP) to determine the appropriate consistencies of fluid for each patient. A video fluoroscopy swallow study (VFSS) is carried out to look closely at the swallowing process. The VFSS will test your ability to drink safely and comfortably. If you have trouble swallowing, you may be at risk for aspiration. Aspiration occurs when food or drink enters the windpipe, potentially going into the lungs. Aspiration may put you at risk for developing an infection of the lungs, called aspiration pneumonia. Even swallowing problems may also put you at risk for not getting enough liquids or food (dehydration or malnutrition). So based on information from the study, the SLP, and doctor will tell how thick liquids (consistency) should be for you to swallow safely.

In 2002, the American Dietetic Association established the National Dysphagia Diet (NDD) guidelines for thickened dietary supplements. This Task Force proposed viscosity ranges for thin, nectar-thick, and honey-thick and spoon thick liquids. To ensure safety during oral administration, patients with dysphagia require an appropriate oral dosage form or modification of the dosage form. The objective of this work is to prepare and evaluate eatable dosage form for the treatment in dysphagia patients using a polymer.

MATERIALS AND METHODS

Preparation of Oral thin film

Film was prepared by using specified polymer by solvent casting method. The specified amount of polymer was weighed and dissolved in specified amount of water for overnight to get a uniform dispersion of 0.4 % to 2 % (w/v) solution respectively. Drug, sodium starch glycolate, vanilline and sodium saccharine were dissolved in specific amount of water in a beaker. The drug solution was added to the polymer solution and mixed using magnetic stirrer for 1 hour. The resulting solution was degassed so as to remove any bubbles formed.

The bubble free solution was casted on to a petri dish of surface area 28.6 cm^2. It was dried for 24 hours at room temperature. The film was removed from the petri dish very carefully and observed for any imperfections. Film that was clear and bubble free was selected for further studies. Film of area 2.25 cm^2(1.25 X 1.25) was cut and stored in a butter paper covered with aluminum foil and stored in a desiccator. Composition of various formulations is shown in table no 1.

Preparation of Edible gels

- Gellan gum powder was dispersed in 50 ml of distilled water maintained at 95°C. The dispersion was stirred at 95°C for 20 min using a magnetic stirrer to facilitate hydration of gellan gum.
- The required amount of mannitol was added to the gellan gum solution with continuous stirring and the temperature was maintained above 80°C. drug was added with stirring.
- Then mannitol, citric acid and methyl paraben were added with stirring.
- Finally, required amount of sodium citrate was dissolved in 10 ml of distilled water and added to the mixture.
- At last flavor was added.
- The weight of the gel was monitored continuously during manufacturing and finally it was adjusted to the 100 gm with distilled water.
- The mixture was allowed to cool to room temperature to form gel. The gels were prepared using five different concentrations of gellan gum (0.1, 0.2, 0.3, 0.4, and 0.5%), each with two different sodium citrate concentrations (0.3 and 0.5%).

Formulation Development of oral thin films

Oral thin films containing Desloratidine were prepared by casting method. The films of sodium alginate and xanthum gum were prepared with an objective to dissolve the film in the mouth. 1.5% sodium alginate and 0.7 % of xanthum gum films were exhibited desired mouth dissolving time and other film parameters, compared to other concentrations of films i.e<1% sodium alginate have poor film forming capacity and >1% of xanthum takes lots of time for drying and which were difficult to remove and having low strength and exhibited unacceptable mouth dissolving time. Hence 1, 1.5, 2 w/v% of sodium alginate and 0.4, 0.7 w/v% concentrations of xanthum films were used for the study.

Propylene glycol (5 % w/w of polymer) was used as plasticizer and to enhance the tensile strength of film.2 % sodium starch glycolate is used as disintegrant to dissolve the films rapidly when comes in contact with saliva. 1 % w/w Sodium saccharine was used as a sweetener and 1 % w/w of vanilin was used as flavoring agent.

Formulation development of edible gel

Desloratadine edible gel formulations were prepared by varying concentrations of gellan gum from 0.1% to 0.5%, lower concentrations i.e 0.1 and 0.2% of gellan gum does not form a gel, and these two formulations were fluid in consistency. 0.3% and above concentrations of polymer showed good physical and rheological properties. As the polymer concentrations increased dissolution take more time due to the entrapment of drug in polymer. So concentrations of polymer and cross linking agent are main criteria in this formulation development.

Table 1.Formulation of edible gel

S.No	Ingredients	EG-1	EG-2	EG-3	EG-4	EG-5	EG-6	EG-7	EG-8	EG-9	EG-10
1	Drug (mg)	100	100	100	100	100	100	100	100	100	100
2	Gellan gum (%)	0.1	0.1	0.2	0.2	0.3	0.3	0.4	0.4	0.5	0.5
3	PEG 400(%)	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
4	Citric acid (%)	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
5	Mannitol (%)	30	30	30	30	30	30	30	30	30	30
6	Sucralose (%)	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
7	Sodium citrate (%)	0.3	0.5	0.3	0.5	0.3	0.5	0.3	0.5	0.3	0.5
8	Methyl parabin (%)	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
9	Flavour (%)	2	2	2	2	2	2	2	2	2	2
10	Water (upto % w/w)	100	100	100	100	100	100	100	100	100	100

	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
API	5mg	5mg	5mg	5mg	5mg	5mg	5mg	5mg	5mg	5mg	5mg	5mg
Na.Alginate *	0.4	0.7	1	1.5	2	--	--	--	--	--	0.5	1
X.Gum*	--	--	--	--	--	0.4	0.7	1	1.5	2	0.5	1
SSG	2	2	2	2	2	2	2	2	2	2	2	2
PG**	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%
Vannilin	1	1	1	1	1	1	1	1	1	1	1	1
Na. saccharine	1	1	1	1	1	1	1	1	1	1	1	1
Water	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
API	5mg	5mg	5mg	5mg	5mg	5mg	5mg	5mg	5mg	5mg	5mg	5mg
Na.Alginate *	0.4	0.7	1	1.5	2	--	--	--	--	--	0.5	1
X.Gum*	--	--	--	--	--	0.4	0.7	1	1.5	2	0.5	1
SSG	2	2	2	2	2	2	2	2	2	2	2	2
PG**	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%
Vannilin	1	1	1	1	1	1	1	1	1	1	1	1
Na. saccharine	1	1	1	1	1	1	1	1	1	1	1	1
Water	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs

RESULT S AND DISCUSSION

Preformulation studies: API Characterization

Description

Melting point of drug was determined and the results were illustrated in the following table

Table 2. Description of Desloratidine (API)

Test	Description
Colour	A white to off white colour powder
Odour	Odourless

The results were found as per specifications**.**

Solubility

These tests were performed as per procedure and the results are illustrated in the following table.

Table 3. Solubility of Desloratidine (API) in various solvents.

Solvents	Solubility
Water	Slightly soluble
pH6.8 Phosphate buffer	Soluble
Methanol	Freely soluble
Ethanol	Freely soluble
Propylene Glycol	Freely soluble

Desloratadine is slightly soluble in water, soluble in pH6.8 Phosphate buffer and freely soluble in alcohols like Methanol, Ethanol and Propylene glycol.

Melting Point

This test is performed as per procedure (8.1.3) and the result was illustrated in the following table.

Table 4. Melting point of API's

Material	Melting Point	Melting Point Range
Desloratidine	150^0c	150-151^0c

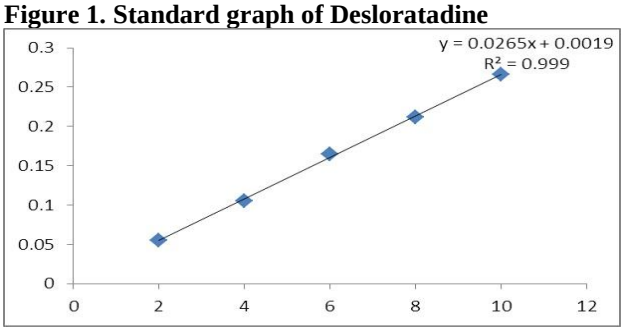
The Result was found to be within limit.

Calibration curve of Desloratidine

Table 5. Standard calibration curve of Desloratidine in pH7.4

Concentration in mcg	Absorbance at 242nm ±SD, n=3
2	0.055±0.011
4	0.105±0.012
6	0.165±0.014
8	0.212±0.012
10	0.266±0.016

Figure 1. Standard graph of Desloratadine



Calibration curve was carried out as per the procedure. Standard graph of Desloratadine in pH 7.4 Phosphate buffer saline shows linearity in the concentration range of 5 - 30 µg/ml with correlation coefficient of 0.999 and the slope was found to be 0.0265.

Drug-Excipient Compatibility Studies: The drug – excipient compatibility studies were carried out by FTIR

Compatibility studies were performed using IR spectrophotometer. The IR spectrum of pure drug and physical mixture of drug and excipients were studied. The characteristic absorption peaks were obtained and as they were in official limits, the drug is compatible with excipients

Evaluation Parameters

Weight variation of the films:

Discussion: Three Films each of 0.35 square inch were cut at three different places from casted films and weight variation was measured. Weight variation varies from 18.65 ± 0.016 to 25.21 ± 0.089. The results of weight variations are shown in the Table-13.

Thickness of the film

The thickness of the film was measured using digital Vernier Calliper with a least count of 0.01 mm at different spots of the film. The thickness was measured at three different spots of the film and average was taken and SD was calculated. It was observed that as the polymer concentration increases the thickness of the film also increases.

Folding endurance of the films

The folding endurance was measured manually. A strip of film 2.5 cm^2 was cut and subjected for the folding endurance studies until it broke at the same place. Folding endurance increases with increase in polymer concentration. The no of times the film fold until it broke was reported.

All batches were showed good folding endurance, as polymer concentration increases folding endurance is also increased. Folding endurance is also a measurement of plasticizer concentration but here all formulation has same concentration of plasticizer, so polymer concentration effect was easily studied in this research work.

Disintegration time

The disintegration time of the film was done by using tablet disintegration test apparatus.

Disintegration times of the films were found to be increased with increase in the concentration of the polymer. The formulation F4 shows 18 Sec (disintegration time) as shown in the table 17. As the polymer concentration increases disintegration time was decreased in these formulations. F4 formulation showed good disintegration time along with good folding endurance property.

Mouth dissolving time

The mouth dissolving time was determined by using beaker containing 7.4-pH phosphate buffer. A size of 2.25 square inch film was subjected for this study. The mouth dissolving time of the film was reported in the Table-18. This mouth dissolving time is directly proportional to disintegration time. Here we can check the dissolution time but specifically in saliva pH.

Each film contain 5 mg / 2.25 sq.cm

The prepared film formulations were analyzed for drug content and it was observed that all the formulation found to contain almost uniform quantity of drug as per content uniformity studies indicating reproducible technique.

***In-vitro* dissolution**

The dissolution study was carried out using USP Type I (Basket type) dissolution apparatus. The dissolution was carried out in 500 ml of pH 7.4 phosphate buffer maintained at 37 ± 0.5^0C at 50 rpm. 5 ml aliquots of samples were taken at various time intervals which were replaced with same volume of fresh pH 7.4 phosphate buffer maintained at 37 ± 0.5^0C. Desloratidine in the samples was then determined spectrophotometrically at $\lambda_{max}$of 242 nm. The results were expressed in table no 20.

Formulations F1 to F3 all showed 100% drug release with in 10min but they are failed in folding endurance and tensile strength. Even formulations F1 to F3 have casting problems, they are not easy to remove from petridish as they are very thin so yield is not good. As polymer concentration increases tensile strength and folding endurance were improved for a formulation but dissolution takes much time, so optimization of formulation is based on the folding endurance, disintegration time and dissolution profile. Formulations F5 also showed good folding endurance but dissolution profile is better in F4 compared to F5 formulation.

Formulations F7 to F10 showed good folding and tensile properties. In these formulations F7 showed good dissolution profile compared to other formulations. F6 formulation is thin and problem in casting. Formulations F9 and F10 formulations have casting problems, they are thick and take much time for drying.

Formulations F11 and F12 were prepared by using combination of these two polymers (sodium alginate and xanthum gum) but these two formulations were not given the desired release pattern, tensile strength and appearance.

From all these formulations it was concluded that F4 formulation with 1.5% sodium alginate showed good folding endurance, tensile strength, disintegration time and drug release profile withno casting problems and good appearance.

Stability studies

The stability studies of the optimized batch F4 was carried out at Room temperature and 8^0C. The films were found to be unacceptable at Room temperature. Films stored at Room temperature were unstable within 1 week period by developing color change (slight yellow) and becoming sticky in appearance. Films stored at 8^0C were found to be stable for 3 weeks. The batch was found to be acceptable visually, mechanically, with slight change in in-vitro disintegration time. The above observations indicate that temperature and humidity plays a critical role in the stability of the rapidly dissolving films containing Sodium alginate as the film forming polymer. Therefore, precautions would be required during packaging and selection of packaging container would play a crucial role for stability of the Oral thin films.

Appearance

The results of evaluation of Desloratadine edible gel batches. All the batches of edible gels were transparent in appearance. The gel of batches EG1, EG2, EG3, EG4, EG5 and EG6 were non-sticky and non-gritty while the gel

of batches EG7 and EG8 were slightly sticky and non-gritty. EG9 and EG10 batches were sticky and slightly gritty. The non-gritty nature of the batches may be due to the suitable concentration of gellan gum and sodium citrate but EG10 was gritty due to higher concentration of gellan gum and sodium citrate.

Consistency

Gellan gum has a good gelling power hence it can produce gels at low concentration. Table no. shows, batches EG1 to EG4 exhibited fluid like consistency while the gels of batches EG6 to EG10 were thick in consistency. As the consistency of gels depends on the concentration of the polymer, batches EG6, EG7 and EG8 had acceptable consistency. These visual inspection results are supported by the viscosity measurements.

Viscosity

Viscosity is the one important parameter which provides vital information during the optimization of the edible gel. The results of evaluation of Desloratadine gellan gum edible gel batches MG1-MG8 are shown in Table no.

The viscosity of the batches EG1 to EG4 were low because of its fluid like consistency while the viscosity of the batches EG9 and EG10 were high because they were very thick in consistency. But, viscosity of batch EG6, EG7 and EG8 were near to in house specification and spoon thickness consistency. As batches EG9 and EG10 were thick in consistency, sticky and gritty, they failed to give good mouth feel. The viscosity of the batches EG6, EG7 and EG8 were acceptable supported by their acceptable consistency. The consistency and viscosity of the edible gels are related to each other because both are dependent on concentration of gellan gum, sodium citrate, and co-solute.

Effect of concentration of co-solute (mannitol and sucralose) on the viscosity and consistency of all the batches of the edible gel was same because it was constant in all the batches. It is clearly evident from the results that changes in the viscosity and consistency of soft gel is greatly because of change in concentration of gellan gum and slightly because of change in concentration of sodium citrate. Free carboxylate groups are present in the structure of gellan gum; therefore gellan gum is anionic in nature and thus it would undergo ionic gelation in the presence of both divalent and monovalent cations such as Ca++, Mg++, K+, Na+, and H+ from acid. However, its affinity for divalent cations such as Ca2+ and Mg2+ is much stronger than monovalents such as Na+ and K+. Therefore, gels of batch EG5 to EG10 were selected for further studies under drug content and in vitro dissolution studies.

pH

The pH of the most stable Desloratidine in aqueous phase is in between 4 and 9. It is also reported that the apparent viscosity of gellan gum dispersion can be markedly increased by increase in both pH and cation concentration. Therefore, the pH of the formulated gels was adjusted and maintained in between 5 and 7 with help of buffering agents such as citric acid and sodium citrate. The amount of citric acid was kept minimum i.e, just to adjust the required pH. Sodium citrate was selected as a salt to contribute cation because it also act as sequestrant, buffering agent and helps in maintaining mechanical property of the gel. The pH of gels of batches EG1 to EG10.

Syneresis

Syneresis is one of the major problems associated with low acylatedgellan gum gels. Syneresis means contraction of gel upon standing and separation of water from the gel. Syneresis is more pronounced in the gels where lower concentration of gelling agent is used. Syneresis was not noticed at room temperature probably due to binding of free water by co-solute. Batches EG6 to EG10 were not showed any syneresis but EG5 slightly showed syneresis.

Drug Content

The drug content of all batches of edible gel was within the acceptable limit.

***In vitro* Dissolution studies**

The results shown in table no. reveal that gels of the batches EG5 to EG10 were exhibited acceptable consistency and viscosity. Thus, they were subjected to dissolution study to draw any conclusion and their percentage drug release at different time intervals has been shown Resultsshow that EG5 and EG6 had good drug release but consistency is not good. EG7and EG8 showed good drug release and also good consistency in these two batches EG8 showed very good consistency and spoon thickness viscosity over EG7 batch and very similar drug release compared with EG7. There was no significant difference between release profiles of the EG7 and EG8, but release profile of batch EG7 does not meet the spoon thickness consistency. Also, viscosity of the batch EG8 batch showed good spoon thickness consistency compared to EG7 which may increase the mouth feel, thus batch EG8 was chosen as the optimized batch.

Stability studies

The results of short-term stability studies, shown in Table no. , indicated insignificant changes in pH, viscosity, and appearance in the optimized formulation with time. Precipitation of desloratadine in the soft gels was not observed in any of the gels. Also, syneresis was not observed in any of the samples at both temperatures. Therefore, it is recommended that edible gel should be stored at about 25°C.

Comparison of optimized formulations of oral thin films and gels

Optimized formulation F4 of oral thin film and EG8 of edible gels dissolution was compared in figure no. and it clearly shows that almost similar in dissolution profiles. But from stability studies it was very clear that storage and packaging of films need additional care

compared to edible gels. Films with natural polymer sodium alginate were unstable at room temperature and unacceptable due to their color and stickiness, whereas edible gels were very stable at room temperature and acceptable at that temperature. Patient compliance is also better for edible gels due to their appearance and ease of administration.

Table 6. Comparative evaluation of Weight variation of oral thin films

S.NO	Formulation code	Average weight of the 2.25 square inch film in mg
1	F1	18.65±0.016
2	F2	22.31±0.011
3	F3	19.21±0.009
4	F4	22.54±0.011
5	F5	18.67±0.026
6	F6	23.31±0.061
7	F7	21.21±0.069
8	F8	24.74±0.031
9	F9	20.65±0.036
10	F10	20.31±0.061
11	F11	25.21±0.089
12	F12	24.54±0.021

*Standard deviation, n =3

Table 7. Comparative evaluation of Thickness of oral thin films

S.No	Formulation code	Average thickness in mm
1	F1	0.22 ± 0.025
2	F2	0.29 ± 0.01
3	F3	0.18 ± 0.00
4	F4	0.23 ± 0.01
5	F5	0.14 ± 0.02
6	F6	0.16 ± 0.01
7	F7	0.21 ± 0.01
8	F8	0.27 ± 0.01
9	F9	0.26 ± 0.01
10	F10	0.23 ± 0.01
11	F11	0.27 ± 0.01
12	F12	0.26 ± 0.01

*Standard deviation, n =3

Table 8. Comparative evaluation of folding endurance of oral thin films

S.No	Formulation code	Folding endurance (no of folds)
1	F1	20 ± 2.08
2	F2	26 ± 4.16
3	F3	28 ± 6.25
4	F4	32 ± 6.02
5	F5	40 ± 8.14
6	F6	18±11.01
7	F7	23 ± 2.15
8	F8	26 ± 3.60
9	F9	27±11.01
10	F10	30 ± 3.15
11	F11	26 ± 2.60
12	F12	29 ±1.01

*Standard deviation, n =3

Table 9. Comparative evaluation of Disintegration time of oral thin films

S.No	Formulation code	Disintegration time in Sec
1	F1	16± 2
2	F2	15 ± 2
3	F3	17 ± 1
4	F4	18 ± 1.15
5	F5	26 ± 3.05
6	F6	32 ± 1.52
7	F7	22 ± 1
8	F8	29 ± 0.53
9	F9	31 ± 1.52
10	F10	48 ± 1
11	F11	19± 0.57
12	F12	26± 2

Table 10. Comparative evaluation of Mouth dissolving time of oral thin films

S.NO	Formulation code	Mouth dissolving time in Sec
1	F1	18± 2
2	F2	17± 2
3	F3	21± 1
4	F4	24± 1.15
5	F5	30± 3.05
6	F6	38± 1.52
7	F7	26 ± 1
8	F8	35 ± 0.53
9	F9	40 ± 1.52
10	F10	53 ± 1
11	F11	26± 0.57
12	F12	33± 2

*Standard deviation, n =3

Drug content uniformity of films

Table 11. Results of drug content uniformity of oral film formulations

S.No	Formulation code	Drug content in mg
1	F1	99.4 %
2	F2	98.2 %
3	F3	95.6 %
4	F4	99.8 %
5	F5	99.2 %
6	F6	99.8 %
7	F7	98.4 %
8	F8	96.2 %
9	F9	95.6 %
10	F10	93.8 %
11	F11	99.2 %
12	F12	97.8 %

*Standard deviation, n =3

Table 12. Comparative evaluation of *Invitro* dissolution profiles of oral thin Films

S.No	Time in min	Cumulative % of drug release					
		F1	F2	F3	F4	F5	F6
1	2	58	55	48	**41.2**	38.6	29
2	4	81	78	78	**73.3**	72.6	58
3	6	99.2	95.8	91.4	**88.9**	86.3	82
4	8	-	99.4	98.5	**96.3**	91.4	88
5	10	-	-	99.2	**98.9**	95.4	95.1
6	12	-	-	-	-	99.2	98.4
7	14	-	-	-	-	-	99.2
8	16	-	-	-	-	-	-
9	18	-	-	-	-	-	-
10	20	-	-	-	-	-	-

Table 13. Drug release graphs of formulation F1 to F6 .Dissolution profile of Oral thin films

S.No	Time in min	Cumulative % of drug release					
		F7	F8	F9	F10	F11	F12
1	2	26	22	18	16	38	29
2	4	53	45	37	29	69	54
3	6	78	71	69	39	75	72.5
4	8	93	85	72.4	48	84.8	80.0
5	10	96.3	92	80.3	56	92.3	89.4
6	12	97.3	93.9	89.	63.4	98.6	95.1
7	14	98.4	95	94.4	75.8	-	98.2
8	16	98.6	96.4	96.8	88.2	-	-
9	18		97.2	98.2	94.3	-	-
10	20		99.6	98.8	96.4	-	-

Table 14. Stability data of optimized formulation F4

S No	Time	Appearance		*In Vitro* Disintegration Time (sec)	
		0-8^{0}C	Room temperature*	0-8^{0}C	Room temperature*
1	1st week	Transparent and acceptable	Slightly yellow and acceptable	18	17
2	2nd week	Transparent and acceptable	Slightly yellow and sticky	19	16
3	3rd week	Transparent and acceptable	Slightly yellow and sticky	18	12

Results of edible gel

Table 15.Evaluative parameter of Edible Gel

S.No	Evaluation parameters	EG-1	EG-2	EG-3	EG-4	EG-5	EG-6	EG-7	EG-8	EG-9	EG-10
1	pH of gel	5.63	5.68	5.58	5.67	5.70	5.75	5.78	5.80	5.68	5.73
2	Appearance	NS,NG	NS,NG	NS,NG	NS,NG	NS,NG	NS,NG	SS,NG	SS,NG	S,SG	S,SG
3	Viscosity (cps)	512	837	1563	2089	3876	5026	5907	7023	8342	9681
4	Consistency	---	---	--	--	-	+	++	++	+++	+++
5	Drug content	100	102	101	102	99	98	98	99	99	99

*NS- Non Sticky, NG- Non Gritty, SS- Slightly Sticky, S – Sticky, SG- Slightly Gritty. Indicates fluidity, + indicates spoon thickness.

Table 16. Drug release profiles of edible gel formulations

Time(min)	EG-5	EG-6	EG-7	EG-8	EG-9	EG-10
2	63	62	59	53	46	39
4	85	83	80	72	65	60
6	93	91	89	88	80	74
8	98	97	95	93	89	85
10	99	99	98	99	95	90
12	99	99	98	99	98	93

Table 17. Stability data of optimized formulation EG8

	1st week		2nd week		3rd week	
At temperature(0-8^0)	5.80pH	7023cps	5.76pH	7029cps	5.71pH	7031cps
At Room temperature*	5.78pH	7028cps	5.73pH	7032cps	5.70pH	7035cps

*Room temperature

Figure 2. FTIR Spectra of Desloratidine pure drug

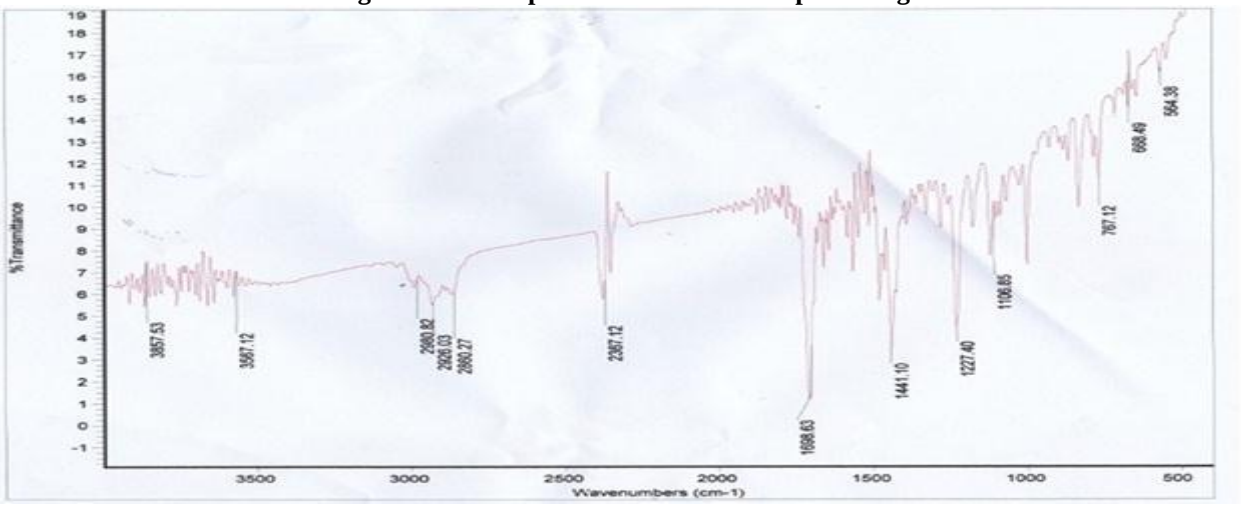


Figure 3. FTIR Spectra of optimized formulation of Desloratidine film

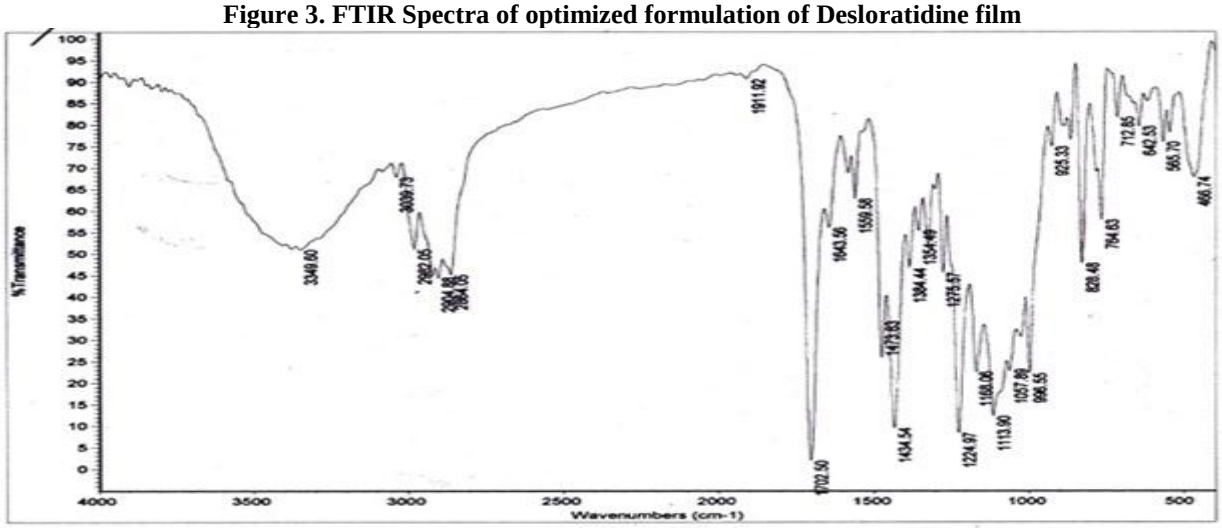


Figure 4. FTIR of optimized formulation of Desloratidine edible gel

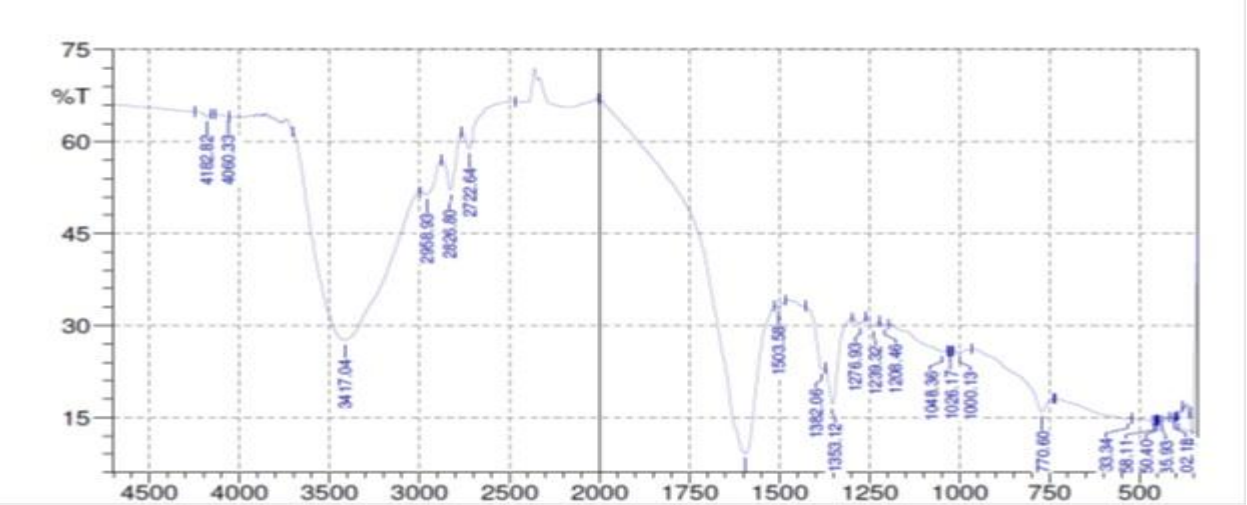


Figure 5. Drug release graphs of formulation F1 to F6

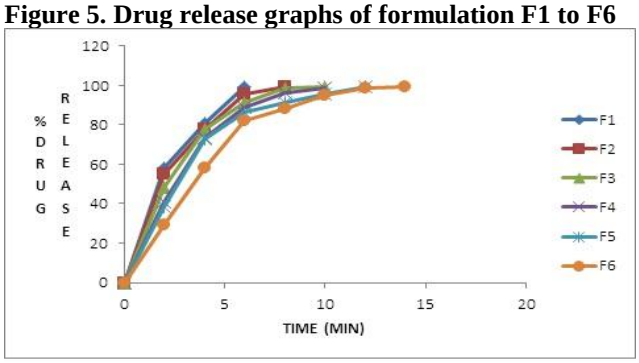


Figure 6. Drug release graphs of formulations F7 to F12

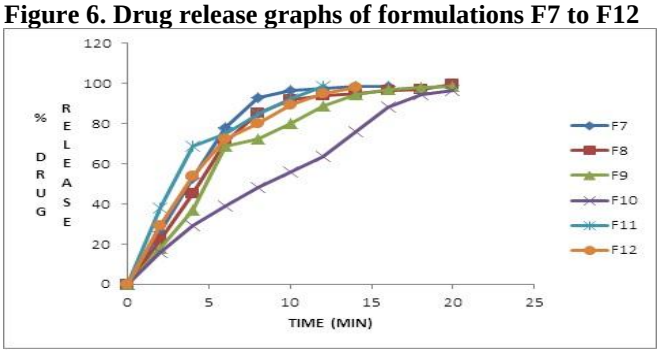


Figure 7. *In vitro* drug release profile of edible gel formulations

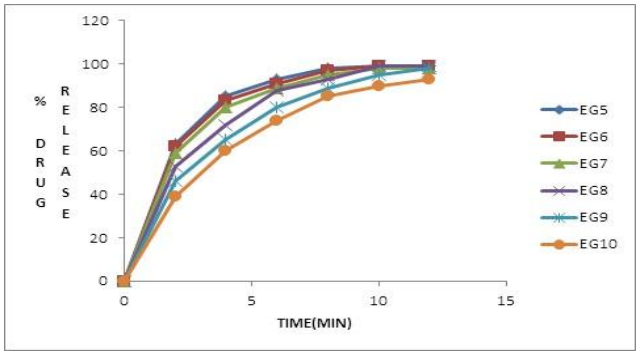
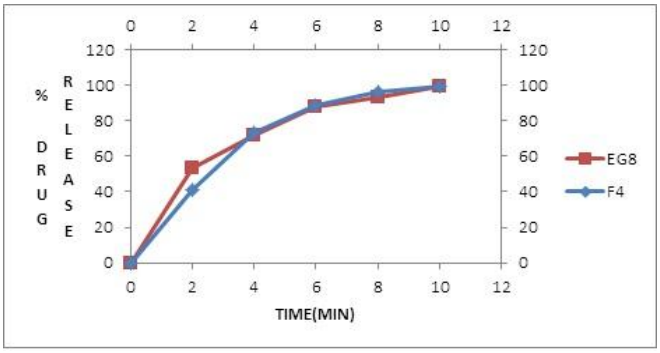


Figure 8. *Invitro* drug release comparison of both F4 and EG8 formulations



CONCLUSION

From this research it was concluded that F4 formulation of desloratadine oral thin films were good in oral thin formulations and EG8 formulation of desloratadine edible gel was best in edible gel formulations. In these oral thin films and edible gel preparations EG8 formulation of edible gel is very better due to its patient's compliance, yield, stability-storage requirements and along with these good properties edible gel shows drug release profile very similar to oral thin films.

FUTURE WORK

Possibility of these formulations in large scale production and their development, extensive stability studies and IVIV correlation studies.

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