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Research Article

# FORMULATION AND EVALUATION OF FAST DISSOLVING ORAL FILMS OF FLUVASTATIN SODIUM BY USING TASTE MASKING TECHNIQUES

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## ABSTRACT

Fluvastatin sodium, a HMG-COA reductase inhibitor has shorter half life (1.2). It undergoes extensive first pass metabolism, frequent dosing is required in case of conventional dosage form. It is an bitter drug so an attempt was made to mask the taste by using three masking techniques. The present investigation indicates the possibility of developing Fluvastatin sodium loaded fast dissolving oral films to enhance the oral bioavailability by avoiding first pass metabolism to provide a rapid onset of action. Solvent casting method was used to formulate the fast dissolving oral film. Different formulation F1–F6 was prepared by using Artificial Sweetening Agents and Flavors (Sucrose, Saccharin); by using Viscosity Modification Method (CMC, Sucrose, Saccharin); by using β-cyclodextrin complexed drug Freeze Drying Method (Cyclodextrin, Sucrose, Saccharin). All the formulation were subjected to evaluation by various parameter like visual inspection, weight variation, folding endurance, film thickness, disintegration time, drug content, *in vitro* drug release, taste masking evaluation. Result obtained indicates all formulation F1-F6 were thin, smooth, flexible and uniform in drug content, weight and thickness as observed with low S.D. values. F6 be the best formulation from drug content, % release, taste masking effect and all other parameters. % release for F6 was found to be 99.6% within 150 sec (2.5 min) which falls within the limit as per pharmacopoeia (5-20 min) for oral dissolving films. Hence indicates quick onset of action within seconds as the oro mucosal absorption of the drug occurs directly from the site of administration to systemic circulation avoiding first pass metabolism to produce the desired action i.e offered significant results in terms of improving taste and bioavailability.

**Keywords:** Fluvastatin sodium, Freeze Drying Method, taste masking techniques, *in vitro* drug release.

## INTRODUCTION:

The oral route of administration is the most preferred route due to its many advantages like ease of administration, accurate dosage, self-medication, pain avoidance, versatility and patient compliance. Tablets and capsules are the most popular dosage forms. But one important drawback of such dosage forms is dysphasia or difficulty in swallowing. This is seen to afflict nearly 35% of the general population. Fast dissolving drug delivery system is a new generation delivery system also known as fast dissolving/disintegrating film for the oral delivery of the drugs which came into existence in the late1970's as an alternative to tablets, capsules, syrups and other formulations for paediatric and geriatric patients, who experience difficulties in swallowing traditional solid dosage forms which combines both the advantages of conventional tablet and of liquid formulation. FDDS is easy to administer and provides better patient compliance in the elderly, paediatric, mentally retarded, nauseated and uncooperative patients. This delivery system consists of the solid dosage forms that dissolve quickly i.e. within a matter of seconds in the oral cavity without the administration of water. The delivery system consists of a very thin oral strip which is simply placed on the patient's tongue or any other oral mucosal tissue and instantly gets wetted by saliva. The film rapidly hydrates onto the site of application. It then rapidly dissolves and disintegrates to release the medication for oro-mucosal absorption. Fast dissolving oral thin films are widely accepted by patients and also to the caregiver for their ease-of-delivery, portability and accurate dosing. The robustness of the film depends upon the type and amount of polymer used and general dissolution time for orally dissolving film is 5–20 minute as per pharmacopoeia. They also provide quick onset of

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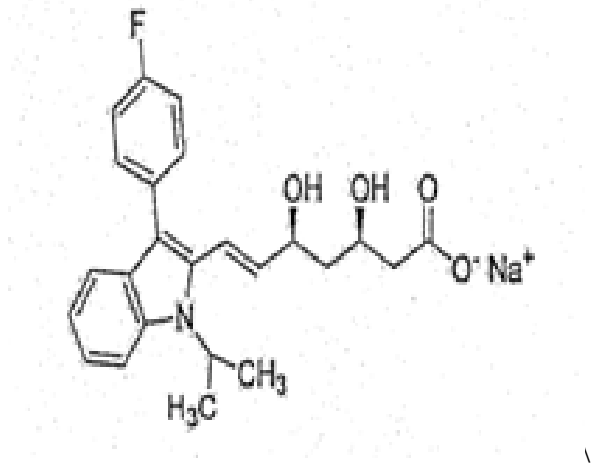
action within few seconds as the oro-mucosal absorption of drug occurs directly from the site of administration to the systemic circulation avoiding first pass metabolism to produce the desired effect [1-3].

Fluvastatin is an antihyperlipidemic agent that competitively inhibits hydroxyl methyl glutaryl-coenzyme A (HMG-CoA) reductase. HMG-CoA reductase catalyzes the conversion of HMG-CoA to mevalonic acid, the rate-limiting step in cholesterol biosynthesis. Fluvastatin belongs to a class of medications called statins and is used to reduce plasma cholesterol levels and prevent cardiovascular disease. It is also the first entirely synthetic HMG-CoA reductase inhibitor and is structurally distinct from the fungal derivatives of this therapeutic class. Chemically it is (R*, S*-(E))-(±)-7-(3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2- yl)-3, 5-dihydroxy-6-heptenoic acid, monosodium salt (M.wt 433.46; M formula $C_{24}H_{25}FNNaO_4$) [4-6].




**Fluvastatin Sodium**

The objective of present study was to design and optimize the dissolving film of Fluvastatin Sodium by solvent casting method using HPC, CMC, sucrose/saccharin, glycerol, pipermint oil, dye (Amaranth), citric acid for obtaining a film with satisfactory characteristics. Different formulation F1–F6 was prepared, by using different techniques in order to improve the taste and bioavailability of Fluvastatin Sodium i.e. by using artificial sweetening agent and flavor (Sucrose, Saccharin); by using Viscosity Modification Method (CMC, Sucrose, Saccharin); by using Freeze Drying Method (cyclodextrin, Sucrose, Saccharin) [6-12].

## Material and Equipments

### Materials

Fluvastatin sodium was purchased from sigma laboratories, via Magus Laboratories, Mohali. Hydroxy propylcellulose, Carboxy methyl cellulose, 2 hydroxy propyl-beta-cyclodextrin were obtained from Otto Chemika Biochemika reagents and Loba Chemie, Pvt, Ltd.

### Equipments

Magnetic stirrer (Tanco), Oven (PLT125A/Tanco), Lyophillizer (Spectrachro Instruments), pH meter (Delux), Screw gauge (Forbes), Dissolution apparatus (Electrolab), modified disintegration apparatus, UV Spectrophotometer model 1800 (Shimadzu, Japan), sieves (ASTM std-best instrument and sieves), Freeze drier (Allied Frost), Millipore (Direct-Q).

### Calibration Curve of Fluvastatin Sodium

Primary stock solution of 100µg/ml was prepared separately in methanol, acetonitrile, distilled water and phosphate buffer respectively. For preparation of different concentrations, aliquots of stock solution were transferred into series of 10ml volumetric flasks and volumes were made with respective solvent to obtain range of 10-60µg/ml of fluvastatin sodium. The $\lambda_{max}$ of fluvastatin sodium was finalized by scanning suitable dilutions of stock in same solvent between 200- 400nm.

### Preparation of Fast Dissolving Oral Films of Fluvastatin Sodium

Fast dissolving oral films of Fluvastatin was prepared by solvent casting technique by using artificial sweetening agents (F1-F2). Firstly water soluble polymers are dissolved in water at 1000rpm. All the other excipents like color, flavoring agent etc are dissolved separately. Then both the solution obtained is mixed thoroughly at 1000rpm for 1 hr. Then a fixed volume of 2ml polymeric solution was taken. Then drug was added to the above polymeric solution (2ml) and stirred for 1 hour. The solution was then casted on the glass moulds and dried in oven at 60 $^0$C. Dried films were removed and stored in desiccator till further use. Same procedures were followed for the preparation by using viscosity modification technique (F3-F4; CMC& Sucrose, CMC & Saccharin) [6-10].

By using freeze drying technique (F5-F6; Cyclodextrin & sucrose, Cyclodextrin & Saccharin); firstly physical mixture of Fluvastatin and β-cyclodextrin in a molar ratio of 1:1 were added to 500ml of double distilled water and stirred for 5 days. The suspension was freeze dried. The freeze dried complex was pulverized and sieved through < 35µm [10]. The composition of drug loaded film is shown in Table 1.

**Table 1: Composition of Fluvastatin Sodium containing Fast Dissolving Oral Films.**

| **Ingredients** | | **F1** | **F2** | **F3** | **F4** | **F5** | **F6** |
|---|---|---|---|---|---|---|---|
| Fluvastatin Sodium (mg) | Drug | 20 | 20 | 20 | 20 | 20 | 20 |
| HPC (mg) | water soluble polymer | 450 | 450 | 450 | 450 | 450 | 450 |
| Sucrose (mg) | Sweetening agent | 27 | - | 27 | - | 27 | - |
| Saccharin (mg) | Sweetening agent | - | 27 | - | 27 | - | 27 |
| Vanilla (mg) | Flavoring agent | 45 | - | | | | |
| CMC (mg) | Viscosity enhancer | | | 22.5 | 22.5 | | |
| Cyclodextrin (mg) | Complexing agent | | | | | 20 | 20 |
| Peppermint oil (% polymeric wt) | | - | 10 | 10 | 10 | 10 | 10 |
| Glycerol (% polymeric wt) | Plasticizer | 20 | 20 | 20 | 20 | 20 | 20 |
| Dye (Amaranth) (mg) | Coloring agent | 4.5 | 4.5 | 4.5 | 4.5 | 4.5 | 4.5 |
| Citric Acid (mg) | saliva stimulating agent | 27 | 27 | 27 | 27 | 27 | 27 |

**Evaluation Parameters [6-10]**

**Weight variation**: Ten films were randomly selected and their average weight was obtained. Individual films were weighed and compared with the average weight for the deviation.

**Thickness**: The thickness of film was measured by micrometer screw gauge at different strategic locations (at least 5 locations; centre & four areas around the edges) and mean thickness was calculated. This is essential to determine uniformity in the thickness of the film as this is directly related to the accuracy of dose in the film.

**Folding endurance test**: Folding endurance was determined by repeated folding of the film (2 x 2 $cm^2$) at the same place till the film breaks or visual crack is observed or folded upto 300 times to determine the flexibility of each film. The number of the times of the film is folded without breaking is computed as the folding endurance value

**Drug Content**: A film was cut into three pieces of equal diameter were taken in graduated glass stoppered flask containing 10 ml of pH 6.8 phosphate buffer. The flask was charged on rotary flask shaker for 24hrs. The solutions were filtered, suitably diluted and analyzed at 305nm in a UV Spectrometer. The average of drug content of three films was taken as final reading. Limit of content uniformity is 85-115%.

**Surface pH**: The surface pH of the films was determined in order to investigate the possible side effects due to change in pH in vivo, since an acidic or alkaline pH may cause irritation to the buccal mucosa. The film to be tested was placed in a Petri dish and was moistened with 0.5 ml of distilled water and kept for 1 h. The pH was noted after bringing the electrode of the pH meter in contact with the surface of the formulation and allowing equilibrating for 1.0 min. This study should be done on at least six films of each formulation and their mean± S.D can be calculated.

**Disintegration test**: In-vitro disintegration time was determined visually in a petridish containing 25 ml of pH 6.8phosphate buffer with swirling every 10 sec. The disintegration time is the time

when the film starts to break or disintegrate. The disintegration time limit of 30 seconds or less for orally disintegrating tablets described in CDER guidance can be applied to fast dissolving oral film. Disintegration time will vary depending on the formulation but typically the disintegration range from 4 to 30 seconds. Although, no official guidance is available for oral fast disintegrating films.

**In vitro Drug Release**: The drug release studies were performed with USP dissolution test apparatus. (Paddle method). The USP dissolution apparatus was thermo stated at the temperature of 37±0.5$^0$C and stirred at rate of 50 rpm in a 900ml dissolution medium of pH 6.8 phosphate buffer. The aliquots of 5 ml were withdrawn at the time interval of every 5mins and replaced with equal volume of dissolution medium. The sink condition was maintained throughout the study. The samples were analyzed at 305 nm in a UV-Vis spectrometer and cumulative amount of drug release at various time intervals was calculated.

**Compatibility studies**: The drug-polymer compatibility was confirmed by taking ATR spectrum of drug, polymer and physical mixture of drug-polymer proved that the excipient were compatible with the Fluvastatin sodium.

### Organoleptic test

The desired organoleptic properties a fast dissolving formulation should have are color, flavor, and taste. As the formulation will disintegrate in the oral cavity so it should provide acceptable organoleptic palatable characteristics. Color makes a formulation acceptable among the patients and moreover oral films should have attractive color as they are administered to children. Hence, color of formulation should be uniform and attractive. Color can be evaluated by visual inspection. The other organoleptic property is the odor. The flavor used in the formulation should provide good odor to the formulation. The odor of the polymer, drug, and any other excipient should be masked with use of flavoring agent. Taste is also an important factor which has to be evaluated. To evaluate the taste, special human taste panels are used [10].

### Taste Evaluation of Oral Films:

The taste of oral film was checked by panel method. The study protocol was explained and written consent was obtained from volunteers. In this method, a group of about 5-10 human volunteers was trained for taste evaluation. Numerical values are then assigned to these levels of bitterness (e.g. 0-5). Subsequently, Oral film containing 20 mg of drug was placed on tongue and taste evaluated after 15 seconds and rated on the same scale to assess its bitterness.

**Stability studies**: When the oral film preparation was stored in an aluminum package under normal condition or in a chamber controlled at 40°C and 75% in humidity for 3 months, no apparent changes in the content, form or color of preparations were observed. The contents of were fairly stable ranging from 98.4% to 101.7% during 13 weeks after storage at 30°C and 60% humidity (normal condition), or from 98.0% to 100.4% during the same periods after storage at 40°C and 75% RH humidity(accelerated condition).

### Result and Discussion

### Calibration Curves of Drug

FVS in methanol, acetonitrile, distilled water and phosphate buffer yields a characteristic curve when scanned in ultraviolet wavelength range between 200-400nm. The scan showed absorption maxima at $\lambda_{max}$ 305nm, there is close proximity to maxima reported [60] as shown in figure 9. Thus, observed $\lambda_{max}$ value is identical to theoretical $\lambda_{max}$ value. This indicates the identity and purity of drug. The $\lambda_{max}$ for FVS in methanol was finalized at 305nm and linear curve was obtained in the range of 10-60µg/ml. In statistical analysis of data low value of standard deviation at all concentrations revealed high level of precision.

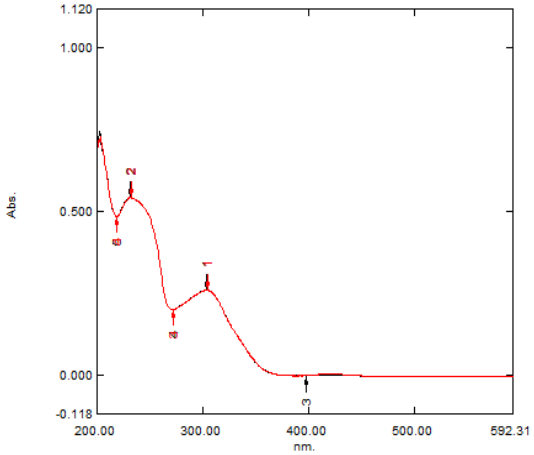



**Figure 1: UV spectrum of 10 µg/ml solution of Fluvastatin in Methanol with $\lambda_{max}$ at 305nm**

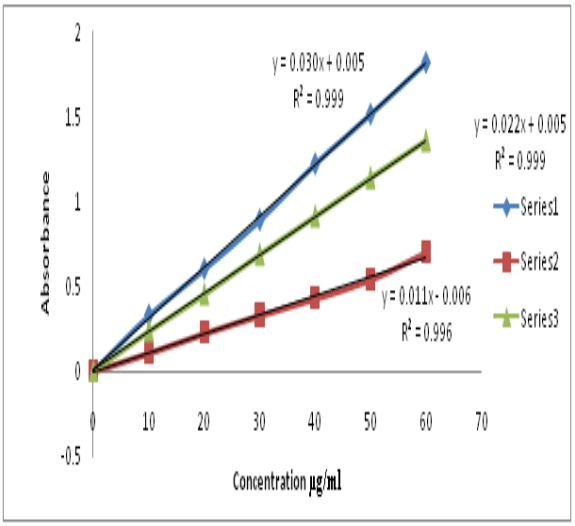



**Figure 2: Calibration Curve of Fluvastatin in MeOH, ACN and Distilled water.**

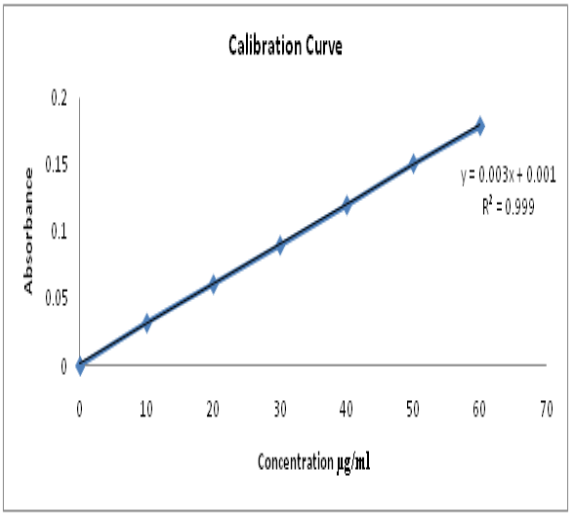



**Figure 3: Calibration Curve of Fluvastatin in Phosphate Buffer**

**Table 2: Characteristics of Calibration Curves of Fluvastatin in various solvents**

| Parameters | Methanol | Acetonitrile | Distilled Water | Phosphate buffer |
|---|---|---|---|---|
| Maximum Absorption ($\lambda_{max}$) | 305 | 305 | 305 | 305 |
| Beer's Law limit (µg/ml) | 10-60 | 10-60 | 10-60 | 10-60 |
| Slope | 0.030 | 0.011 | 0.022 | 0.003 |
| Intercept | 0.005 | 0.006 | 0.005 | 0.001 |
| Correlation Coefficient ($r^2$) | 0.999 | 0.996 | 0.999 | 0.999 |

**Preparation and Evaluation of film formulations**:

All the film formulations containing HPC, CMC, sucrose, saccharin, peppermint oil, glycerol and citric acid were readily prepared by solvent casting method. All the films were evaluated for their physical parameters, and they were found to be flexible, uniform, smooth and transparent. The weight of (21.22cm²) film ranged from 73.7±0.121 to 117.5±0.306 mg. The weight of the films was found to be increase as the concentrations of the polymer increases. The average % deviation of all the formulations was found to be in limit (i.e. less than mg is ± 10%) and hence all the formulation passed the test for weight variation as per official requirements. All film formulations exhibited good folding endurance (>300). Thickness in the different formulation was found in the range of mm. Maximum thickness was found in formulation F1 (0.774±.008 mm), while minimum found in formulation F4 (0.666±.008). Disintegration time of formulation F1-F6 ranges from 20-26 seconds which is within the limit i.e. less than 30 seconds (Table 3).

**Compatibility studies:**

The ATR spectrum showed the characteristic peaks of pure fluvastatin sodium at 1685$cm^{-1}$, 1564$cm^{-1}$, 1405.67, 1337 $cm^{-1}$ , 3067 $cm^{-1}$ and 3630.61 $cm^{-1}$ due to the presence of –C=O, -C=C, -C-N, -C-H, -C-H, O-H respectively. All these characteristic peaks were well present in ATR spectrum of drug with different polymers indicates no interaction between drug and polymers (HPC and CMC) and other excipient as no new peaks were produced. However there was only reduction in intensity of peaks due to dilution of the drug with excipient. This ruled out that the drug is compatible with polymers and stable in formulation.

**Surface pH**

An acidic or alkaline pH of administered dosage forms can irritate the oral mucosa. The measured surface pH was found to be close to neutral in all the formulations which means that they have less potential to irritate the oral mucosa and therefore they should be fairly comfortable.

**Stability studies**:

When the optimized oral film preparation was stored in an aluminum package under elevated temperatures for 3 months; No apparent changes observed in the content, folding endurance, thickness, color of films. There is no significant changes in vitro disintegration and in vitro dissolution studies after 3months.

**Table 3: Physical Parameters of Fast Dissolving Oral Films**

| Formulation Code | Appearance | Weight variation (mg) | Thickness (mm) | Folding endurance | Area($cm^2$) | Disintegration time (seconds) |
|---|---|---|---|---|---|---|
| F1 | Transparent | 73.7±0.121 | 0.774±.008 | >300 | 21.22 | 22sec |
| F2 | Transparent | 76.4±0.209 | 0.756±.005 | >300 | 21.22 | 20sec |
| F3 | Transparent | 102.4±0.285 | 0.758±.008 | >300 | 21.22 | 24sec |
| F4 | Transparent | 105.4±0.209 | 0.666±.008 | >300 | 21.22 | 26sec |
| F5 | Transparent | 112.4±0.280 | 0.758±.008 | >300 | 21.22 | 26sec |
| F6 | Transparent | 117.5±0.306 | 0.772±.008 | >300 | 21.22 | 25sec |

**Drug Content:**

Fast dissolving film was cut into small pieces and transferred into a graduated glass stoppered flask containing about 10 ml of 6.8 pH phosphate buffers. The flask was charge on rotary flask shaker for 24 hrs. The solution was filter and the amount of drug present is determined by UV spectrophotometric method (305nm). Drug content of the matrices was carried out as to assure that the loading of drug is uniform in formulation. The films were found to contain 97.96±0.288 to 99.60±0.352% content. The average percent deviation of all the formulations was found to be within the limit and hence all the formulations passed the test for content uniformity as per official requirements. From the result obtained it was clear that there was proper distribution of drug in all formulations. Hence it was concluded that the drug was uniformly distributed in all formulations with acceptable deviation. The drug content analysis of prepared formulations showed that the process employed to prepare films was capable of giving uniform drug content with minimum batch variation. F6 shows maximum drug content (Figure 4)

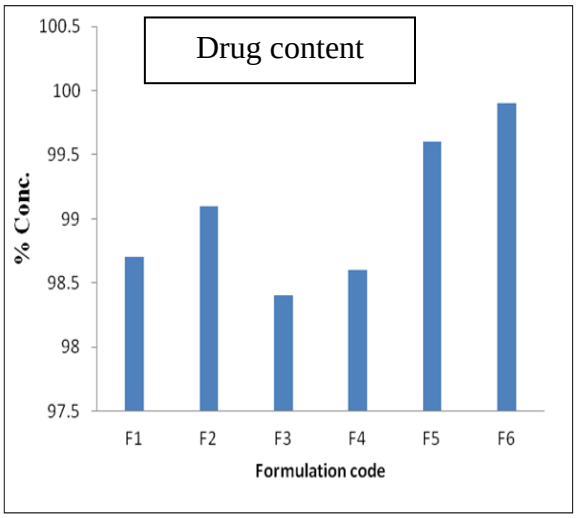



**Figure 4: Drug Content of Oral Films**

**In Vitro Drug Release:** Dissolution studies of films were performed by U.S.P. XXIII type II apparatus in 6.8 phosphate buffer (500ml) and 0.1N HCl (500ml). The temperature required is 37±0.5°C and the rotation speed should generally be 50 rpm. The samples are needed to withdrawn at various time intervals and analyzed spectrophoto-metrically.

Release studies are required for predicting the reproducibility of rate and duration of drug action.

The result of in-vitro study shows maximum release i.e. 99.6 % at 150 seconds in F6 formulation. Although all other prepared formulations also shows more than 96% release within 150 sec i.e. 2.5 min (Figure 5).

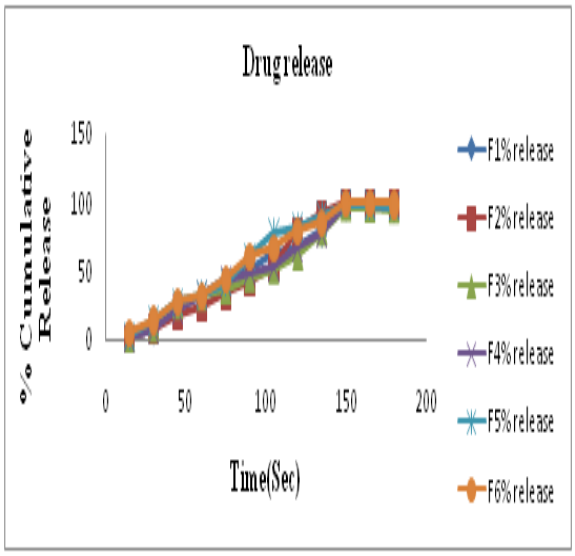



**Figure 5: Cumulative % Drug Release Profile of Fluvastatin Sodium Fast Dissolving Oral Films of formulations F1-F6**

Data obtained from dissolution values revealed that drug release from formulation followed first order kinetics. In vitro stability evaluation with different environmental conditions, confirms the potential of films for longer storage.

**Data analysis: Kinetic Data / Model fitting**:

The *In vitro* data was fit to different equations and kinetic models to explain permeation profiles. Model fitting data was represented in. The coefficient of correlation of each of the kinetics was calculated and compared. From the Regression coefficient value it was concluded that it follows first order kinetics (Figure 6). The data was further treated as per Higuchi's equation (Figure 7) indicated that the drug released by diffusion predominated with the formulation.

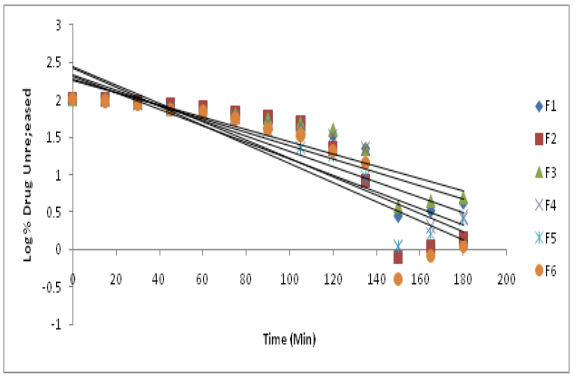



**Figure 6: First Order Plots of Fluvastatin Sodium Fast Dissolving Oral Films of Formulations F1-F6**

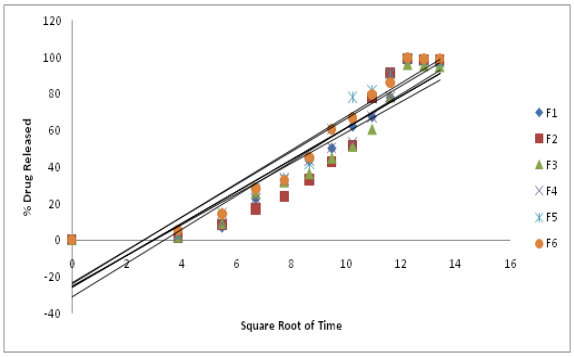



**Figure 7: Higuchi Plots of Fluvastatin Sodium Fast Dissolving Oral Films of Formulations F1-F6**

## Taste Evaluation: Panel Method

The taste of oral film was checked by panel method. The study protocol was explained and written consent was obtained from volunteers. In this method, a group of about 5-10 human volunteers was trained for taste evaluation. Numerical values are then assigned to these levels of bitterness (e.g. 0-5). Subsequently, Oral film containing 20 mg of drug was placed on tongue and taste evaluated after 15 seconds and rated on the same scale to assess its bitterness. F6 shows better result of taste masking (Table 4).

**Table 4: Evaluation of Taste of Fast Dissolving Films**

| Formulations | Volunteer 1 | Volunteer 2 | Volunteer 3 | Volunteer 4 | Volunteer 5 |
|---|---|---|---|---|---|
| F1 | 2 | 2 | 1 | 2 | 1 |
| F2 | 0 | 1 | 2 | 0 | 1 |
| F3 | 1 | 2 | 1 | 0 | 0 |
| F4 | 1 | 0 | 2 | 1 | 0 |
| F5 | 1 | 0 | 1 | 0 | 0 |
| F6 | 0 | 1 | 0 | 0 | 0 |

0= palatable, 1= normal, 2=slightly bitter, 3=bitter, 4= extremely bitter, 5= Beyond bitter.

**Table 5: Parameters after accelerated stability study of formulation F6**

| Parameters after accelerated stability study of formulation | | Temperature maintained at 40±2°c; relative humidity (RH) maintained at 75±5%RH | | |
|---|---|---|---|---|
| | Initial | After 1 Month | After 2 Month | After 3 Month |
| Drug Content (%) | 99.60±0.05 | 99.15±0.25 | 98.67±0.15 | 97.89±0.48 |
| In vitro drug release (%) | 99.60±0.08 | 99.30±0.21 | 98.81±0.14 | 97.60±0.10 |

## Conclusion

This study shows that it is possible to formulate fast dissolving films of Fluvastatin sodium prepared using different techniques by the solvent-casting method which is simple and cost effective with improved patient compliance. All the formulation were subjected to evaluation by various parameter like visual inspection, weight variation, folding endurance, film thickness, disintegration time, drug content, *in vitro* drug release, taste masking evaluation. Result obtained indicates all formulation F1-F6 shows good result from which formulation F6 be the best formulation from drug content, % release, taste masking effect and all other parameters. % release for F6 was found to be 99.6% within 150 sec which falls within the limit as per pharmacopoeia (5-20 min) for oral dissolving films. Hence indicates quick onset of action within seconds as the oro mucosal absorption of the drug occurs directly from the site of administration to systemic circulation avoiding first pass metabolism to produce the desired action. In the present work, it can be concluded that the fast dissolving films formulation can be an innovative and promising approach for the delivery of Fluvastatin for the treatment of hyperlipidemia.

## REFERENCES


1. Thakur N, Bansal M, Sharma N, Yadav G and Khare P. Overview "A Novel Approach of Fast Dissolving Films and Their Patients". Advances in Biological Research. 2013; 7(2): 50-58.
2. Siddiqui N.M.D, Garg G and Sharma P.K. A Short Review on "A Novel Approach in Oral Fast Dissolving Drug Delivery System and Their Patents". Advances in Biological Research. 2011; 5(6): 291-303.
3. Panda B.P, Dey N.S and Rao M.E.B. Development of Innovative Orally Fast Disintegrating Film Dosage Forms: A Review. International Journal of Pharmaceutical Sciences and Nanotechnology. 2012; 5(2): 1666-1674.
4. Farooq S.A, Saini V, Singh R, Kaur K. Application of Novel Drug Delivery System in the Pharmacotherapy of Hyperlipidemia. Journal of Chemical and Pharmaceutical Sciences. 2013; 6(3): 138-146.
5. Kumar H.K, Althaf S.A, kumar B.K, Ramunaik M, Suvarna C.H. A Review on Hyperlipidemic. International Journal of Novel Trends in Pharmaceutical Sciences. 2013; 3(4): 59-71.
6. Sharma S and Lewis S. Taste Masking Technologies: A Review. International Journal of Pharmacy and Pharmaceutical Sciences. 2010; 2(2): 6-13.
7. Sagar T, Amol G, Dengale R, Patil P, Sharma Y. Review on: Taste Masking Approaches and Evaluation of Taste Masking. International Journal of Pharmaceutical Sciences. 2012; 4(2): 1895-1907.
8. Sharma V, Chopra H. Role of Taste and Taste Masking of Bitter Drugs in Pharmaceutical Industries An Overview. International Journal of Pharmacy and Pharmaceutical Sciences. 2010; 2(4): 14-18.
9. Sharma D, Kumar D, Singh M, Singh G, Rathore M.S. Taste Masking Technologies: A Noval Approach for the Improvement of Organoleptic Property of Pharmaceutical Active Substance. International Research Journal of Pharmacy. 2012; 3(4): 108-116.
10. Jagdale S.C, Gawali V.U, Kuchekar B.S, Chabukswar A.R. Formulation and In Vitro Evaluation of Taste-Masked Oro-Dispersible Dosage Form of Diltiazem Hydrochloride. Brazilian Journal of Pharmaceutical Sciences. 2011; 47(4): 908-916.
11. Kumar S.N, Agilandeswari D, Sabitha P, Prathyusha A, Yathiraju K and Chandy V. Fast Dissolving Oral Films: A Novel Drug Delivery System for Diclofenac. Pharma Science

Monitor An International Journal of Pharmaceutical Sciences. 2013; 4(1): 3649

**12.** Gardouh A.R, Ghorab M.M, Badawy S.S and Gales R.B. Preparation and Characterization of Mucoadhesive Buccal Film for Delivery of Meloxicam. British Journal of Pharmaceutical Research. 2013; 3(4): 743-766.