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FORMULATION AND EVALUATION OF TASTE MASKED OFLOXACIN ORAL SUSPENSION

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ABSTRACT

The disagreeable taste of drugs causes difficulties in swallowing causes patients to avoid their medication. Many antibiotics have an extremely bitter oral administration of drugs with obnoxious and bitter tastes with acceptable level of palatability is a challenge in pediatric and geriatric formulation. Suspension helps to pharmacy and medicine by supplying Insoluble and unpalatable substance in the form of acceptable dosage form. Earlier many methods for taste masking have been used which include use of ion exchange resin, complexation and coating of drugs. So, objective behind this study is to formulation and evaluation of taste masked ofloxacin oral suspension. Ofloxacin is a broad spectrum antibiotic for the treatment of Chlamydial and non-gonococci infections. In present work an attempt has been made to mask the taste of ofloxacin by using Indion Ion Exchange resign and suspension is prepared in different six batches. All the batches were evaluated for various evaluation parameters like Drug Content, pH, Bitterness, Viscocity, Sedimentation, Rate and Time and Percentage Drug release. All the batches were shown satisfactory results. The study results showed that formulation batch F5 meet the requirements official standards. Finally it could be conclude that the oral palatable taste masked suspension can be prepared by using Indion Ion Exchange resign for pediatrics and geriatrics patients.

Key Words: - Suspension, Ion-Exchange Resin, Ofloxacin, Indion 204, Indion 234

I. INTRODUCTION

Oral drug delivery is most common and favored by all Patients. Now patients expect and demand formulations that are pleasantly, or at least tolerably, flavored. The disagreeable taste of drugs causes difficulties in swallowing (dysphagia) or causes patients to avoid their medication thereby resulting in low compliance of patients. Many antibiotics especially gatifloxacin, ciprofloxacin, ofloxacin and ornidazole have an extremely bitter taste making oral administration, a difficult task (Srikanth M, Sunil S. and Rao N. 2010, Abraham J., Mathew F. 2014). Oral administration of antibiotics & antibacterials with obnoxious and bitter tastes with acceptable level of palatability is a challenge in pediatric and geriatric formulation (Abraham J., Mathew F. 2014, Rajesh A.M. and Popat, K.M. 2017). A Pharmaceutical suspension is a coarse dispersion in which insoluble solid particles are dispersed in a liquid medium. Suspension helps to pharmacy and medicine by supplying Insoluble and unpalatable substance in the form of acceptable dosage form. In designing a suspension formula a number of factors must be kept in sight. First of all a decision has to be taken whether a flocculated or Non-floculated system has to be evolved. Earlier many methods for taste masking have been used which include use of ion exchange resin, complexation and coating of drugs by various polymers (Bhowmik D.et.al. 2010, Sampath Kumar K.P.et.al.2012). So, objective behind this study is to formulation and evaluation of taste masked ofloxacin oral suspension. Ofloxacin is a broad spectrum antibiotic for the treatment of Chlamydial and non-gonococci infections (Saini P.et.al. 2013 and Suthar A.M. 2010). In present work an attempt has been made to mask the taste of ofloxacin by using Indion 204 and 234 Ion Exchange resign and suspension is prepared in F1, F2, F3, F4, F5 and F6 batches. All the batches were evaluated for various evaluation parameters like Drug Content, pH, Bitterness, Viscosity, Sedimentation rate and time and Percentage Drug release. The study results showed that formulation all batches meet the requirements official standards. Among all batches F5 batch was found most convenient dosage form for palatability, stability and In-vitro release for better management of special patients. Finally it could be conclude that the oral palatable taste masked suspension can be prepared by using Indion 204 and 234 Ion Exchange resign for pediatrics and geriatrics patients.

II. MATERIALS AND METHODS

The pure drug ofloxacin and Indion 204 obtained as gift sample from Concept Pharma. Ltd, and other Sucrose, Sorbitol, xanthum gum, sucralose, methyl paraben, propyl paraben, polysorbate 80 (Tween 80) Sodium carboxymethylcellulose and flavor were purchased from S. D. Fine chemicals (Mumbai, India). All other chemicals/solvents of analytical grade were used.

A. Physical Mixture Compatibility:-

All the prepared batches of Drug Resin complex were prepared for testing drug resin compatibility.

B. Preparation of Drug: Resin Complex*:-*

Accurately weighed quantity of resin as per given in table no.1 was added in 100ml beaker containing specified quantities of water with continuous stirring for 10-15 min. Then accurately weighed quantity of Ofloxacin was dispersed in resin solution and stirred for 3-5 hrs. Mixture obtained after vigorous stirring was used for further formulation of suspension (Suthar A.M. 2010 and Alayoubi A. et.al 2016).

C. Preparation of Suspension*:-*

Initially to prepare base of suspension as per given in table no.1, accurately weighed quantity of sugar was dissolved in specified quantity of previously boiled water and filtered. Then accurately weighed quantities of sorbitol, glycerin, sodium bronidiol, carboxymethylcellulose, citric acid monohydrate, polysorbate 80 (tween 80), propyl paraben and methyl paraben added in sugar solution with continuous stirring. Previously prepared drug resin complex added into sugar solution under with stirring. The reaming material coloring and flavoring agents were added in above solution and stirred for 15min. Final volume of suspension was adjusted by using purified water (Suthar A.M.et.al. 2010, Alayoubi A. et.al 2016 and Suthar A, Patel M. 2011).

III. EVALUATION

A. Physical Mixture Compatibility Study:-

The physical mixtures of Ofloxacin in 1:1 ratio with Resin Inion 204 and 234 and other excipients like Citric Acid Monohydrate sodium carboxymethyl cellulose were prepared and observed for possible physical variations (Rele R. 2015 and Mohite B. et.al.2012).

B. Drug Loading:-

The drug content was noted by assay procedure spectrophotometrically at 291 nm using 0.1 N HCl (pH1.2) as a blank (Shaikh S. et.al. 2012 and Rele R. 2015).

C. Taste Evaluation:-

The taste of Drug resign complex was tested by panel method, 10 human volunteers were selected. About 50 mg of drug equivalent complex material was held on tongue and taste evaluated after 10 second. The responses of volunteers were recorded. The taste given by each volunteer was recorded against pure drug using a numerical scale as a bitterness level using following Parameters (Suthar A.M. et.al. 2010 and Mohite B. et.al.2012).

(3 = Very biter 2 = Bitter; 1 = Slightly Bitter 0 = Normal)

D. Appearance:-The formulated suspensions were visually evaluated for color and appearance.

E. Determination of pH:-The pH of the formulated suspensions was determined by the use of digital pH meter and the results were noted (Suthar A.M. et.al. 2010).

F. Determination of Viscosity:-

Viscosity of suspension was determined by using of Brookfield Viscometer from 0.3 to 100 at different rpm. (Rele R. 2015).

G. Determination of sedimentation volume (F):-

It is determined by using measuring cylinder. Prepared suspension was taken in 100 ml measuring cylinder. The suspension was allowed to settle for hours and the volume of sedimentation was noted. The sedimentation volume can be calculated using equitation (Jain B et.al.2013).

Volume of sedimentation (F) = Ho/Hu ----- Eq.

Where, Ho is original volume of sediment and Hu is final volume of sediment

H. Specific Gravity (Wt/ml :-

Specific gravity of suspensions was determined by standard gravity bottle and with the help of digital weighing balance and the specific gravity was calculated using the Equation (Ito M. etal.2013).

Specific gravity = Weight of Sample/ Weight of water X 0.99602

I. Drug Release Study:-

In-vitro drug releases of the formulated suspension was carried out using USP-type II dissolution apparatus (paddle type). The 900 ml 0.1 N HCl as dissolution medium was placed in bowl at 37+ 0.5^0C and rpm of 50. The 5 ml of suspension dose was placed in each bowl of dissolution apparatus. The dissolution apparatus was allowed to run for 1 hour (60 minutes). Sample measuring 5 ml were withdrawn after every 10 minutes. The dissolution medium was replaced every time with the same fresh quantity of the dissolution medium. Samples after withdrawing were filtered, suitably diluted and analyzed spectrophotometrically at 430 nm and 320 nm using 0.1 N HCl as blank for Ofloxacin. The cumulative percentage drug release was calculated (Malik K et. al. 2011 and Ito M. etal.2013).

IV. RESULTS and DISCUSSION

A. Physical Mixture Compatibility:-

All the prepared physical mixtures were not found any interaction further they evaluated for FTIR spectra study.

B. Fourier Transform Infrared Spectroscopy:-

Infrared analysis of drug was studied for Pure Ofloxacin Pure Ion Exchange Resin and Drug Resin Complex the result showed that there were no interaction was found and the presence of important functional groups in the infrared spectra of drug. The resultant spectra are shown in Figure No. 1, 2 and 3 respectively.

C. Drug Loading:-

The drug content of Drug Resin Complex in all batches were found in range of 87% to 90% range at pH 4. It is given in table no. 4.

D. Taste Evaluation:-

The bitterness of all batches decreased from slight bitter to less bitter it is given in table no. 5.

E. Suspension Evaluation: -

The prepared suspension evaluated for various physicochemical parameters given in table no. 6. All the batches results have shown very attractive appearance. The Viscosity of all batches lies between 148-297 cps range having ease of handling and sufficient sedimentation period. The sedimentation volume of all batches lies between 0.81-0.97 and content of Ofloxacin was 96 to 97 % in all batches. The pH of all batches ranged from 3.6 to 5.33 slightly acidic.

F. *In-vitro* drug release:-

Percentage drug release study of all the batches was calculated and graphically represented below in fig. 4. for batch F1, F2, F3 and fig 5 batch F4 F5, F6. All batches shown marked satisfactory release of Ofloxacin within 60 minutes 95.54 to 98.64 percentage of drug release. The batch F5 containing Indion 234 ion-exchange resin shown 98.22 percentage of maximum drug release in 60 minutes in comparison to other batches.

IV. CONCLUSION

The extremely bitter taste of Ofloxacin was successfully masked using complexation method using Ion-exchange resin Indone 234. The study results exposed that all batches meet the requirements of official standards. Among all batches F5 batch using 1:2 ratio Ofloxacin to Ion-Exchange resin was found most convenient dosage form for palatability, stability and In-vitro release for better management of special patients. Finally it could be conclude that the oral palatable taste masked suspension can be prepared by using Indion 234 Ion Exchange resign for pediatrics and geriatrics patients.

V. ACKNOWLEDGEMENT

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Table No.1 Formulation Table

Name of Ingredients	Formulation code					
	F1	**F2**	**F3**	**F4**	**F5**	**F6**
Ofloxacin	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg
Indion 204	50 mg	100 mg	150 mg	-	-	-
Indion 234	-	-	-	50 mg	100 mg	150 mg
Syrup Base						
Sucrose	2.5 gm	2.5 gm	2.5 gm	2.5 gm	2.5 gm	2.5 gm
Sorbitol solution	250 mg	250 mg	250 mg	250 mg	250 mg	250 mg
Glycerin	750 mg	750 mg	750 mg	750 mg	750 mg	750 mg
Methyl Paraben	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg
Sodium Carboxy Methyl Cellulose	15 mg	15 mg	15 mg	15 mg	15 mg	15 mg
Col. Idacol Sunset Yellow Supra	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg
Polysorbate 80 (Tween 80)	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg
Citric acid monohydrate	2.5 mg	2.5 mg	2.5 mg	2.5 mg	2.5 mg	2.5 mg
Purified water	5 ml	5 ml	5 ml	5 ml	5 ml	5 ml

mg :- milligram, ml:- Mililiter

Table No. 2. Drug-excipient compatibility study at 40±2ºC/75±5% RH

Condition: 40±2ºC/75±5% RH Pack: Glass Vials					
Sr. No.	**Drug + Excipient**	**Physical Evaluation**	**Chemical Evaluation**	**Drug:Excipient ratio**	**Inference**
1.	**Physical mixture of Ofloxacin and Indion 204**	No colour change	No change in FT-IR Spectra	1:1	**Compatible**
2.	**Physical mixture of Ofloxacin and Indion 234**	No colour change	No change in FT-IR Spectra	1:1	**Compatible**
3.	**Physical mixture of Ofloxacin and Sodium CMC**	No colour change	No change in FT-IR Spectra	1:1	**Compatible**
4.	**Physical mixture of Ofloxacin and Citric Acid Monohydrate**	No colour change	No change in FT-IR Spectra	1:1	**Compatible**

FT-IR-Fourior Transformer Infra Red

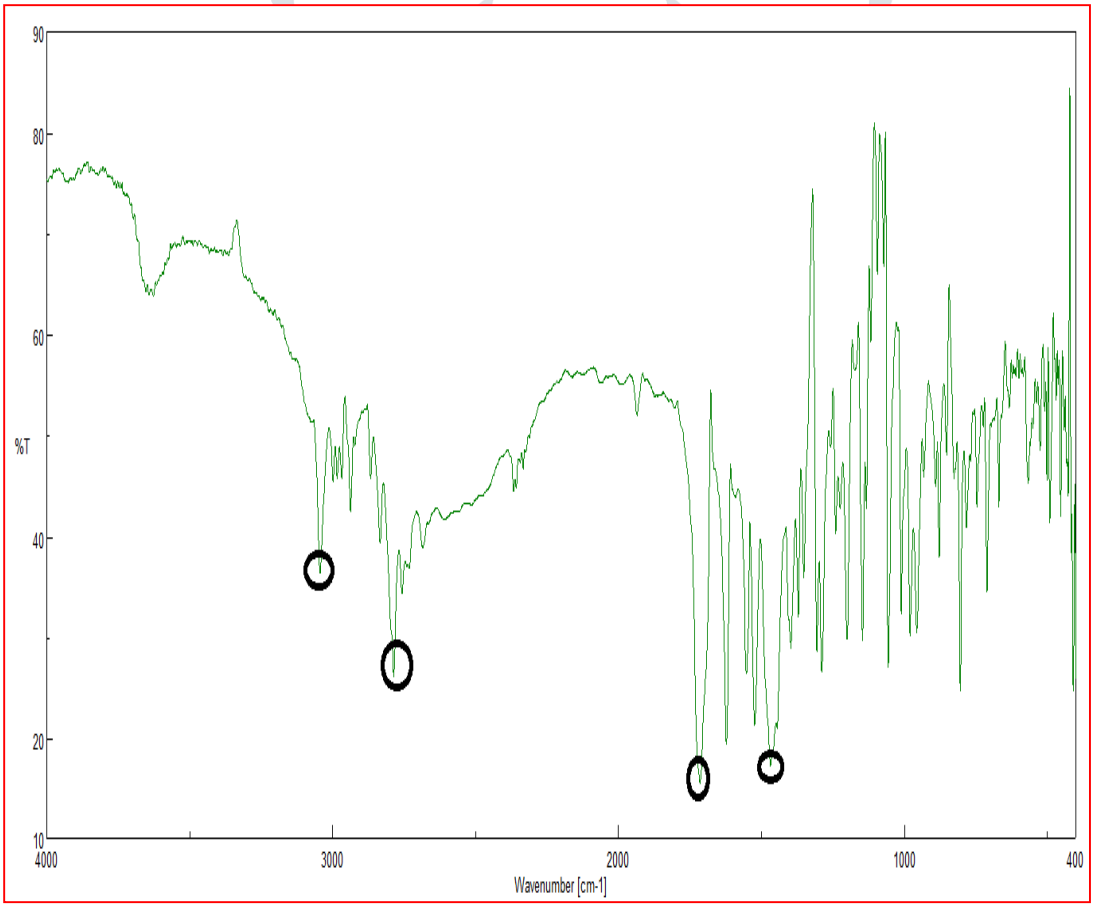
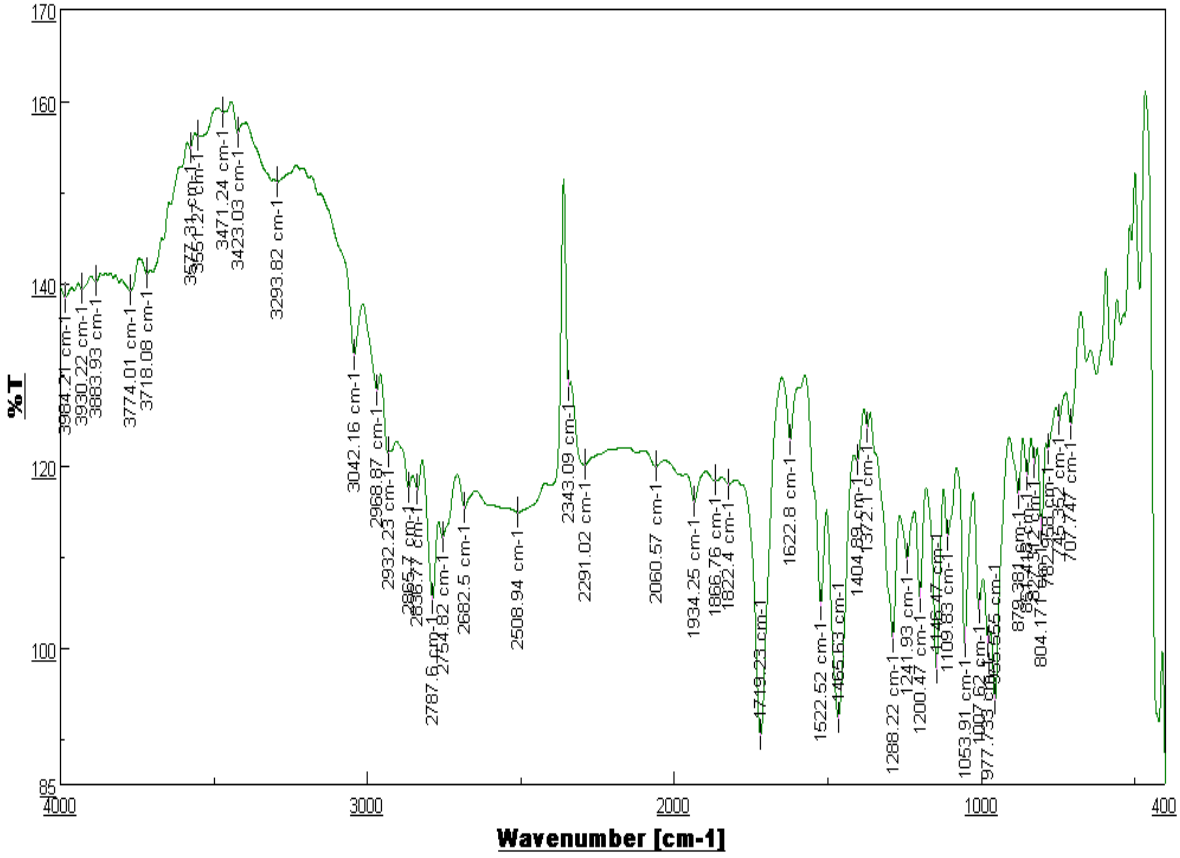


Fig 1. FTIR Spectra of Pure Ofloxacin

Table No. 3 FTIR interpretation of Ofloxacin

Peak cm^{-1}	**Group**	**Type of vibration**
3050-3000	OH	Stretching
2750	Alkyl Groups CH3	Stretching
1650-1600	Quinolone Group N-H	bending vibration
1450-1400	OXO Group C-O-C	Stretching

Fig. 2 FTIR Spectra of Ofloxacin + Indion 204



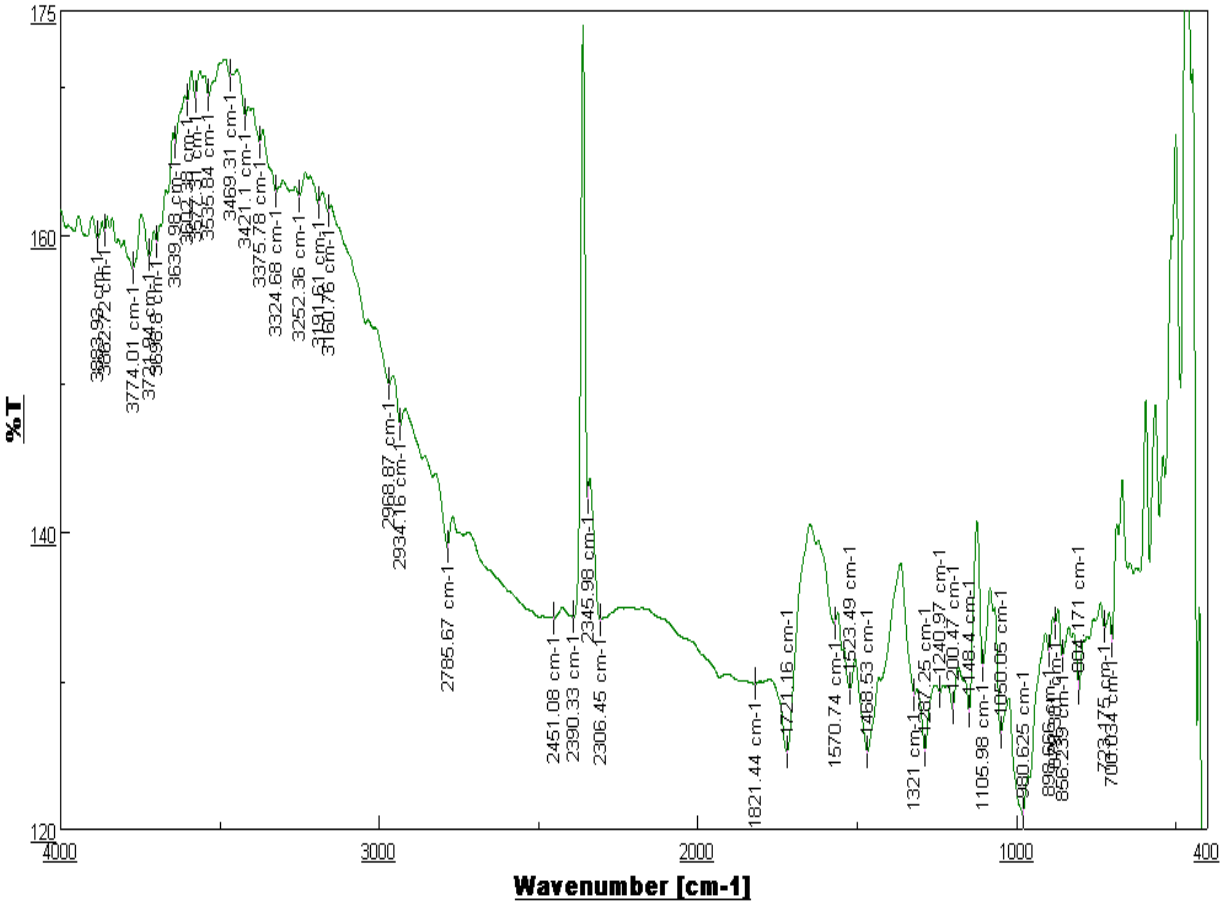


Fig.3 FTIR Spectra of Ofloxacin + Sodium Carboxy Methyl Cellulose

Table No. 4 Percent Drug Loading at pH 4

Formulation	% Drug bound
Ofloxacin: Indion 204 (1:1)	88.41%
Ofloxacin: Indion 204 (1:2)	86.53%
Ofloxacin: Indion 204 (1:3)	87.94%
Ofloxacin: Indion 234 (1:2)	90.32%
Ofloxacin: Indion 234 (1:3)	88.67%

Table No. 5 Bitterness Level After

Volunteers	Bitterness level after					
	10 sec.	1 min.	2 min.	5 min.	10 min.	15 min.
1	X	0	0	0	0	0
2	X	X	0	0	0	0
3	0	0	0	0	0	0
4	0	0	0	0	0	0
5	0	0	0	0	0	0
6	0	0	0	0	0	0
7	X	0	0	0	0	0
8	0	0	0	0	0	0
9	0	0	0	0	0	0
10	0	0	0	0	0	0

Mouth feel: X = Slight bitter, 0 = Bitter less, *Sec:-Seconds, Min: - Minutes*

Table No. 6 Evaluation Parameters

Parameters	Formulation Batches Code					
	F1	F2	F3	F4	F5	F6
Viscosity (cps)	148	220	250	280	298	297
pH	3.66	4.10	4.18	4.27	4.33	4.45
Sedimentation Volume (F)	0.81	0.77	0.90	0.96	0.93	0.97
Wt/ ML (gm/ml)	0.99	1.10	1.12	1.13	1.07	1.18
% DRC	96.45	96.28	99.65	98.80	88.36	68.94
Taste	Bitter	Slight Bitter	Less Bitter	Less Bitter	Less Bitter	Less Bitter
Appearance	Viscous Suspension					

Cps :- Centipoise, Wt/Ml:- Weight per milliliter, gm/ml – gram per milliliter % CDR :- Percent Drug Resin Complex

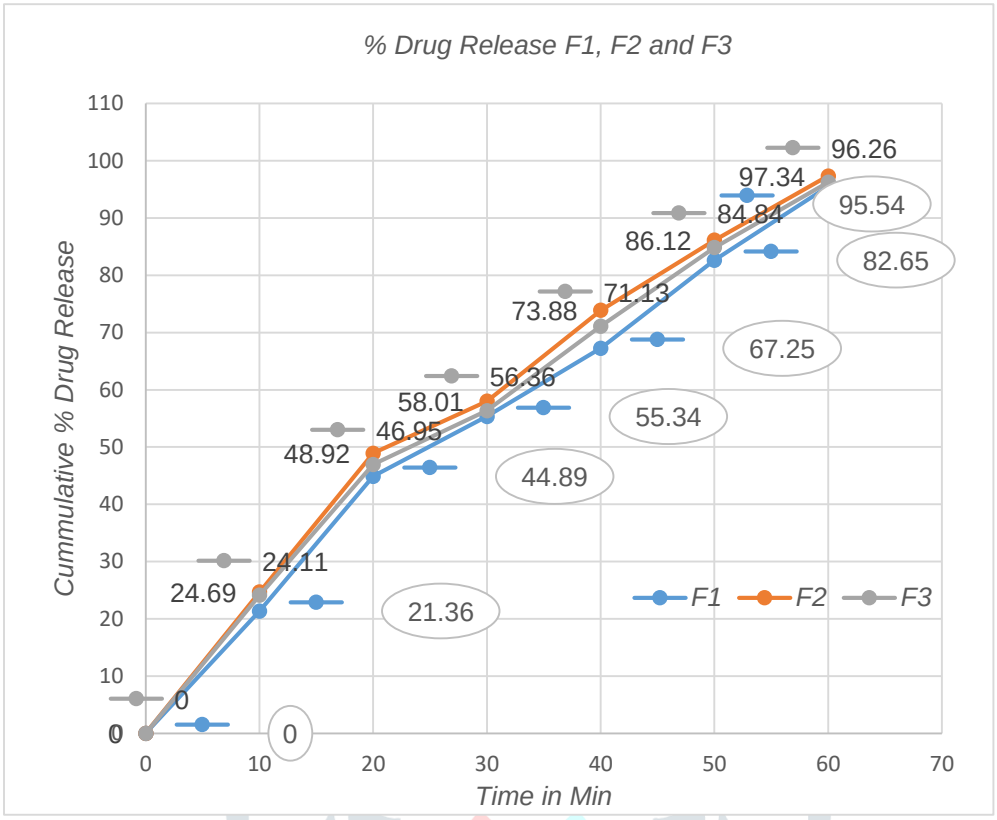


Fig. 4 In-vitro Drug Release Study Batch F1, F2 and F3

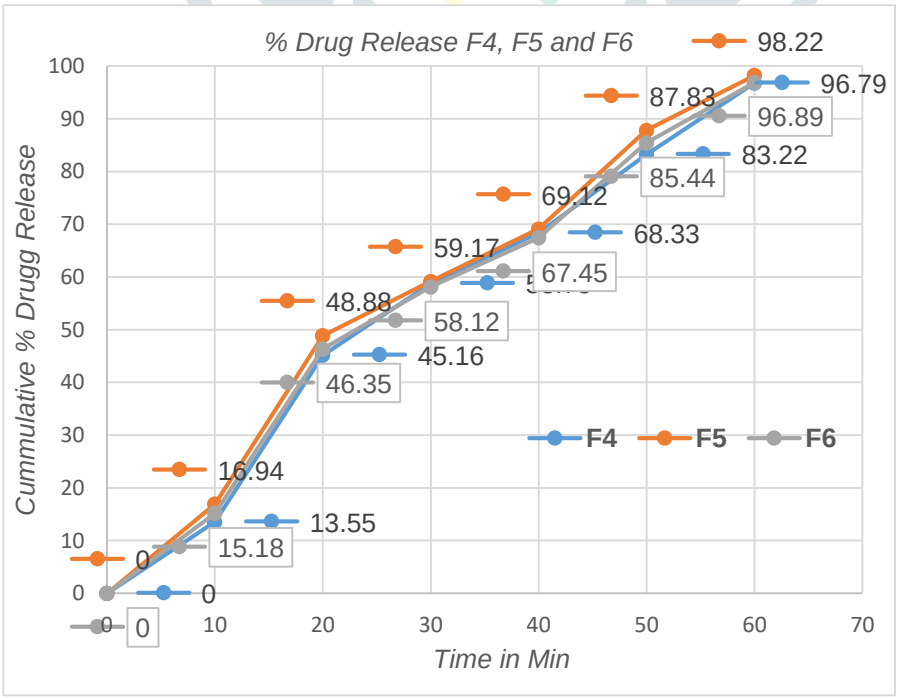


Fig. 5 In-vitro Drug Release Study Batch F4, F5 and F6

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