Formulation & In-Vitro Evaluation of Aminophylline Anhydrous Bioadhesive Tablets

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Abstract:

The formulation of the oral bioadhesive Aminophylline Anhydrous tablet, various hydrophilic polymers and their combinations were used in varying concentrations of mucoadhesive polymer like HPMC K4M, Carbopol 934, Ethyl Cellulose, Aspartame, Talc and Magnesium Stearate added to the formulation are essentially required to achieve in-vitro buoyancy, desirable drug release, and excellent bioadhesive strength. Tablets were subject to various evaluation parameters such as Hardness, Friability, Drug content, Weight Variation and in vitro drug release study. It was revealed that tablets of all batches had acceptable physical parameters. Tablets of batch F8 have good mucoadhesion along with in vitro drug release. It was observed that tablets of all batches followed the equation of Zero, 1st Order Release Kinetics, Korsmeyer and Peppas drug release profiles. Tablets of Batch F8 were selected as an optimum batch. Stability studies revealed that there was no significant change in the hardness, friability, drug content, and dissolution profile of formulation F8. Thus, this formulation was stable at different conditions of temperature. The present study shows that can be used for designing a mucoadhesive CR drug delivery system. Various hydrophilic polymers and their combinations were used in varying concentrations of mucoadhesive polymer like HPMC K4M, Carbopol 934; hence it may increase the therapeutic efficacy of the drug by increasing the bioavailability and patient compliance and stimulates the skeletal muscles.

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Introduction:

Oral controlled release (CR) systems continue to be the most popular ones among all the drug delivery systems [1].

Mucoadhesive delivery systems offer several advantages over other oral CR systems by virtue of prolongation of residence time of drug in the gastrointestinal tract, targeting, and localization of the dosage form at a specific site [1-4].

Also, these mucoadhesive systems are known to provide intimate contact between dosage form and the absorptive mucosa, resulting thereby in a high drug flux through the absorbing tissue [5].

In addition, bio-adhesive dosage forms have been used to target local disorders at the mucosal surface to reduce the overall dosage required and to minimize the side effects that may be caused by the systemic administration of the drugs. Bio-adhesive formulations use polymers as the adhesive component. These polymers are often water soluble and when used in a dry form, they attract water from the mucosal surface and this water transfer leads to a strong interaction. These polymers also form viscous layers when hydrated with water, which increases the retention time over the mucosal surfaces and leads to adhesive interactions [6]. Several studies reported bioadhesive oral drug delivery systems in the form of tablets, films, patches, and gels for oral, buccal, nasal, ocular, and topical routes; however, very few reports on bioadhesive tablets using natural hydrophilic polymers are available. Prolonged contact time of a drug with a body tissue through the use of a bioadhesive polymer can significantly improve the performance of many drugs. In our study, aminophylline anhydrous is used as a model drug. The objective of this study is to develop, characterize, and evaluate

mucoadhesive matrix tablets of aminophylline employing various natural hydrophilic bioadhesive polymers such as HPMC K4M, Carbopol-940, Aspartame, E.C, Lactose for prolonged gastrointestinal absorption. The prepared tablets were evaluated for different parameters such as swelling index, in vitro drug release rates, and in vitro mucoadhesive strength. Aminophylline is the ethylenediamine salt of theophylline. After ingestion, theophylline is released from aminophylline, and theophylline relaxes the smooth muscle of the bronchial airways and pulmonary blood vessels and reduces airway responsiveness to histamine, methacholine, adenosine, and allergen. Theophylline competitively inhibits type III and type IV phosphodiesterase (PDE), the enzyme responsible for breaking down cyclic AMP in smooth muscle cells, possibly resulting in bronchodilation. Theophylline also binds to the adenosine A2B receptor and blocks adenosine mediated bronchoconstriction. In inflammatory states, theophylline activates histone deacetylase to prevent transcription of inflammatory genes that require the acetylation of histones for transcription to begin [7-10].

Materials and Methods

Materials:

Table.1 LIST OF CHEMICALS

S. No.	Chemicals	Brand
1	Aminophylline Anhydrous	Care Formulation PVT LTD Narela, New Delhi
2	HPMC K4M	Amit Trading Company Jhilmil Colony, Delhi
3	Ethyl Cellulose	Jeksan International New Delhi
4	Carbopol-940	NKBR College of Pharmacy & Research Centre Meerut
5	Magnesium Stearate	-
6	Talc	-
7	Aspartame	Advance Inorganics Rohini, Delhi
7	Lactose	Aakriti Trading Company Sheikh Saraj, New Delhi

Table.2 List of Apparatus's used in Formulation

Apparatus's	Manufacture
Punching Tablet Machine	Shakti PharmatechPvt. Ltd, India
UV- Visible Spectrophotometer	Labtronics (Model no. LT2900)

Monsanto Hardness Tester	Kshitij Innovation, India
Friability Testing Apparatus (Single Drum)	Kshitij Innovation, India (Model no. FAT-O23)
Hot Air Oven	Universal Hot Air Oven
pH meter	KshitijPvt. Ltd., Punjab
Dissolution Test Apparatus USP type 2	Electrolab, India, (Model no. USP-TDT 06L)
FT-IR Spectrophotometer	Shimadzu (Model no. IRAffinity-1)

Preformulation Studies:

Standardization of Drug:

Spectrophotometric Method:

The drug was analyzed by using LAB INDIA UV-1800 spectrophotometer having double beam detector configuration. Standard curve was plotted in 0.1N HCL at the maximum wavelength of 274nm [11].

Fourier Transformation Infra –Red Analysis:

Drug- excipients compatibility studies the infra red absorption spectra of unmixed drug & with unalike ingredient were hold in the scale of four hundred thousand to four hundred cm-1 using KBr dise procedure, 1-2 milligram of material to be analyse was mixed with 300-400 mg, specified quantity of minute powder & dried KBr these sum are mainly enough to give a circle of 10-15 diameter and pellet of right strength by a hydraulic press [12].

Micrometries:

Angle of repose:

Mostly funnel was used in this method, firstly weight of the powder and it taken in a funnel, the height (h) funnel was place in a stand, after the powder is place in the funnel to freely flow, then the angle of repose of the powder is find out. Range of repose can zero degree. The angle of repose of the powder is found out the following formula [13].

$$\tan \theta = h/r \quad (1)$$

Therefore, $\theta = \tan h/r$

Here,

θ = angle of repose

h = height of the pile

r = radius of the pile base

Bulk density

Bulk density was calculated by adding a known mass powder to a cylinder. The density was calculated as mass. Tapped density in this method firstly we have to weigh the known powder and

then the known powder transfer in a 10 ml mechanically tapping cylinder. The tapping was started until the little further volume changed was observed [14].

Calculated by following equation

Loosen bulk density = total mass of powder /volume of powder

Tapped bulk density = powder wt. / tapped volume

Carr's index

Carr's index help in measuring the power need to breakdown the friction into the particle & the hopper. Carr's index > 25 % is carefully to be a sign of low flow capability, and under 15, of good flow property It can be calculated by following equation [15, 17].

Carr's index (%) = [(total bulk density –loosen bulk density) ×100]/TBD

Where TBD = tapped bulk density

4.2.3.4 Hausner ratio:

Hausner ratio is an indirect index of ease of powder flow. It is calculated by the following formula.

Hausner's Ratio = Tapped density / Bulk Density

Preparation of Tablets:

Tablets were composed of two layers i.e., Core layer and Backing layer, Core layer contains drug complex made by inclusion complexation, different mucoadhesive Polymers, Lactose, Talc, Magnesium Stearate and Aspartame as a sweetener. This layer weighed about 100mg. Backing layer contains water impermeable compound, ethyl cellulose. The weight of this layer was 50 mg. Therefore total weight of the tablet was 150mg.

Preparation: Direct double compression technique was employed for the formulation. In this technique, first intermediate layer was formed and blend of second layer was placed on first intermediate layer and compressed to get bilayer tablet. Compositions of the core layer contains drug, mucoadhesive polymers.

Evaluation Parameters of all Formulations:

Tablet Hardness:

Tablet hardness was laboratory techniques in this technique we have check the hardness of tablets in case of storage and handling before usage. The hardness of the tablets we can perform by using the hardness tester like Monsanto hardness tester, 6 tablets each batch crushing with known weight was recorded in kg/cm2 and average weight was calculated [18].

Thickness:

Ten tablets were randomly selected and the thickness was measured using a Vernier caliper. Results were expressed as mean±SD.

Friability of Tablets:

Friability was defined as it was capacity of a solid material break into smaller pieces in case of transportation. Friability follows the following procedure. Firstly 20 tablet taken and weight accurately and place in a plastic chamber and set the chamber at 25 rpm for 4 minutes, after the 4

min and 100 revolutions stop the Roche apparatus and reweight the 20 tablets and Calculate the loss in tablet weight by the following formula [19].

% weight loss = initial of tablet – final weights of tablets/ final weights ×100

Weight Variation:

Weight variation was define as to ensure that each of tablet carry proper amount of drug. This method was performed as, weight of 20 individual tablet using analytical balance, after that calculate the average weight of tablet, and after that calculate the individual tablet weight to the average [20].

Drug Content Uniformity:

For this at least 30 tablets were randomly selected. Out of 30 tablets, 10 tablets were crushed into fine powder and assayed individually. The powder was dissolved in 500 ml of 0.1N HCl, filtered and the specific aliquots were taken and analyzed spectrophotometrically (Shimadzu, SPD-10AVP, Kyoto, Japan) at 274nm [21].

In vitro Drug Release Studies:

The USP type II rotating paddle method was used to study the drug release from the bilayer tablet. The dissolution medium consisted of 500ml of pH 6.8 phosphate buffer. The release study was performed at 37 ± 0.5°C, with a rotation speed of 50 rpm. The backing layer of the buccal tablet was attached to the glass slide with cyanoacrylate adhesive. The disk was placed at the bottom of the dissolution vessel. Aliquots were withdrawn at regular time intervals and replaced with fresh medium to maintain sink conditions. The samples were filtered, made appropriate dilutions with phosphate buffer and were thereafter analyzed spectrophotometrically at λmax value of 274nm using a Shimadzu UV-Visible1800 double-beam spectrophotometer. Cumulative percentage drug release was calculated using an equation obtained from a calibration curve which was developed in the range of 5-35mg/ml for pH-6.8 phosphate buffer. The experiment was performed in triplicate [21].

4.6 Kinetic Parameters of all Formulations:

The dissolution view of main acceptable preparation was provide to zero order, 1st order & higuchi model to know the mechanism modelling of liberate the model was adopted for determining the proper model [21].

4.6.1 Zero Order:

A zero order response in few reactions, the measure was adequately equivalent of the reactant concentration the rate of zero order reaction dose not very neither greater nor lowering reactants alternativeness means equal to the rate continual, (k) of the reaction.

4.6.2 First Order Reaction:

First order reaction is defined as that proceeds at a rate on rectilinear on single reactant concentration.

4.6.3 Higuchi Model:

A huge number of modified release formulation have few sort matrix system in such instances, the moiety dissolve from the matrix, the dissolution pattern of drug is dictated by H2O perforation, in this higuchi method, a plot of cumulative % moiety released v/o square root of time is linear.

$$Ft=Kht1/2$$

4.7 Stability Studies:

Stability studies are a most important part of the improving of the life of pharmaceutical dosage form. They allow the evaluation of API Drug product stability studies is finding out of the main acceptable preparation as per international conference of Harmonisation guideline at 40**±2°C/** 75**±** 5%. There is a no major change in the physical and chemical properties of tablet of formulation F5 after 3 months.

Results and Discussion

Preformulation Study:

Melting Point Determination:

It was obtained melting point values 269.5℃by using melting point apparatus.

UV Spectroscopy (Determination of λ max):

After scanning of the sample drug, the wave length is obtained about 274nm in pH 7.2 phosphate buffers by using UV Spectroscopy Method Fig.1.

Table.3 Calibration Curve of Aminophylline Anhydrous

S.No.	Concentration (µg/ml)	Absorbance 274nm
1.	0	0
2.	5	0.1223
3.	10	0.2143
4.	15	0.3487
5.	20	0.4720
6.	25	0.5734
7.	30	0.6823

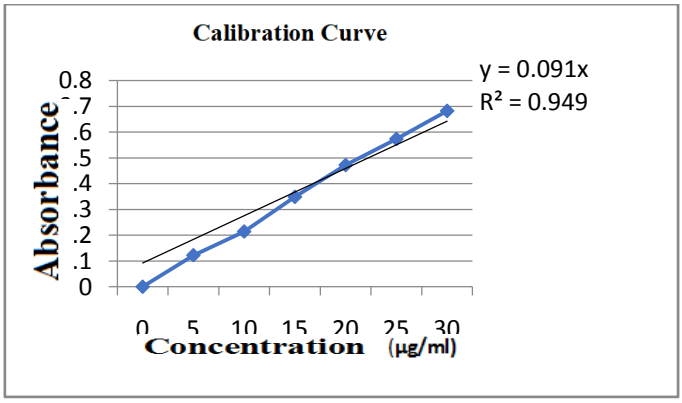

Fig.1. UV light Absorption spectrum of Aminophylline Anhydrous in 0.2 NHCl

Aminophylline Anhydrous showed maximum absorbance in phosphate buffer pH 7.2 at 274nm. The solution obeyed Beer-Lambert's law for concentration range of 0 to 30µg/ml with regression coefficient of 0.949. Standard curve of theophylline prepared in phosphate buffer pH 7.2 is shown in fig.1.

5.2 Powder Flow Properties:

Table.4 Flow Properties

Parameter	Angle of repose (0)	Bulk density (g/ml)	Tap density (g/ml)	Hausner's Ratio	Carr's Index (%)
F1	20.22±0.3	0.388±0.03	0.560±0.02	1.10±0.03	12.51±0.02
F2	23.25±0.6	0.514±0.06	0.584±0.03	1.13±0.05	13.34±0.05
F3	28.12±0.1	0.517±0.03	0.598±0.04	1.10±0.04	11.32±0.06
F4	24.23±0.4	0.521±0.05	0.605±0.01	1.14±0.02	10.31±0.04
F5	27.20±0.2	0.540±0.03	0.615±0.05	1.15±0.06	9.90±0.02
F6	25.19±0.7	0.556±0.06	0.568±0.02	1.12±0.03	14.12±0.03
F7	30.22±0.2	0.565±0.01	0.589±0.03	1.11±0.04	12.65±0.01
F8	21.20±0.5	0.586±0.03	0.578±0.06	1.14±0.05	13.67±0.05

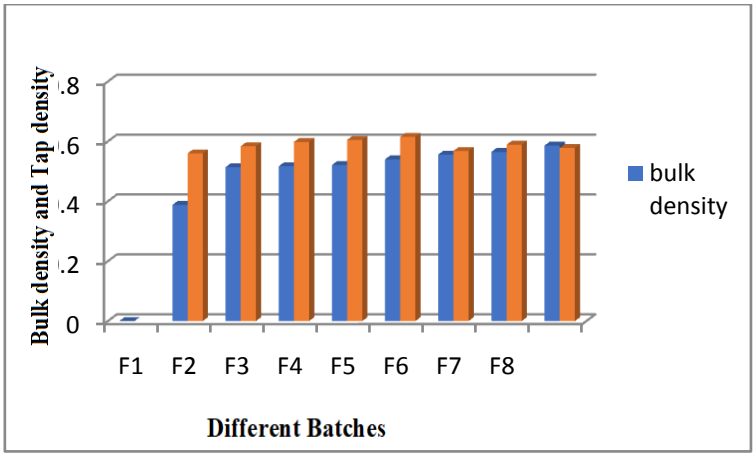

Fig.2 Diagrammatically Representation of Bulk density & Tap Density

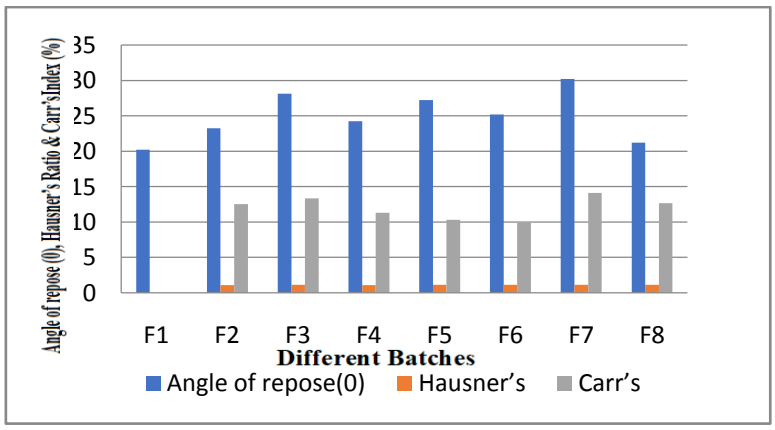

Fig.3 Diagrammatically Representation Angle of repose (0), Hausner's Ratio & Carr'sIndex (%)

FT-IR Spectra:

Dry sample of drug and potassium bromide was mixed uniformly and filled into the die cavity of sample holder and an IR spectrum was recorded using diffuse reflectance FTIR spectrophotometer (Shimadzu FTIR 84005). The results of IR spectra obtained were revealed by figures 03-06. The results depicted that all characteristic peaks of Aminophylline Anhydrous with HPMC K4M, Carbopol-940, Ethyl cellulose and physical mixture of formulation within the range of pure Aminophylline Anhydrous revealing lack of significant interaction between drug and selected polymers for formulation of press coated tablets.

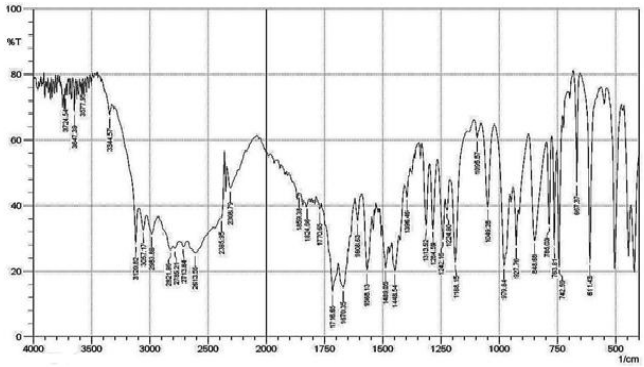

Fig.4 FT-IR Spectra of Aminophylline Anhydrous

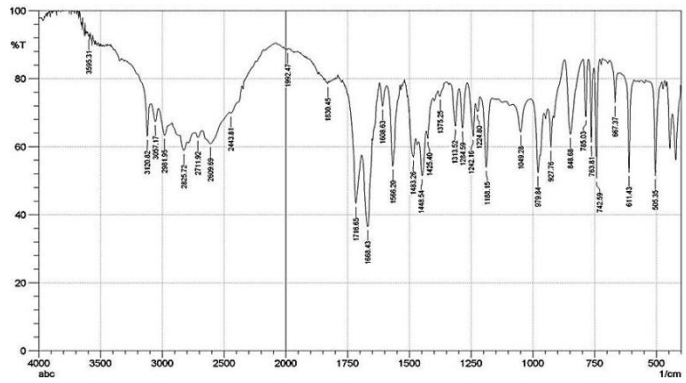

Fig.5 FTIR Spectra of drug and Carbopol-940

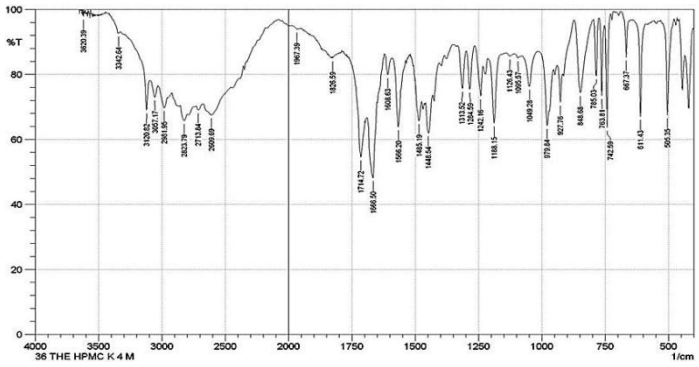

Fig.6 FTIR Spectra of Aminophylline Anhydrous with HPMC K4M

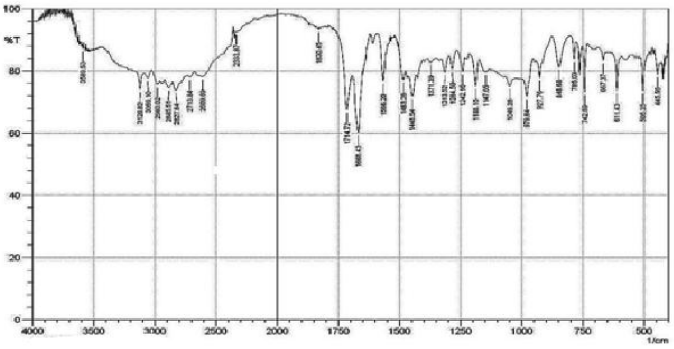

Fig.7 FTIR Spectra of Aminophylline Anhydrous with Ethyl cellulose

Table.5 FT-IR Spectral Data of Pure Aminophylline Anhydrous with Excipients

Functional Groups	**Peaks Observed (wave no. (cm-1))**			
	Aminophylline Anhydrous	**Aminophylline Anhydrous +Carbopol-940**	**Aminophylline Anhydrous + HPMC K4M**	**Aminophylline Anhydrous + Ethyl cellulose**
OH bonding	852.30	852.36	852.11	752.17
C- H bonding	926.4	926.70	928.51	826.32

CH2 stretching	1172.09	1168.56	1051.27	1032.05
O-H stretching	1354.40	1366.36	1268.20	1277.08
NH2 stretching	1510.85	1523.08	1417.59	1437.82
C-H stretching	3235.65	3114.14	3094.88	3084.75
R-O-CH3 stretching	3330.15	3323.07	3225.01	3242.04

Preparation of Aminophylline Anhydrous:

Table.6 Preparation chart of Aminophylline Anhydrous

S.No.	Ingredients (mg)	No. of Formulation							
1.	Aminophylline Anhydrous (mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
		300	300	300	300	300	300	300	300
2.	Carbopol 934	1.60	1.50	1.55	1.50	1.25	1.50	1.50	1.50
3	HPMC-K4M	1.74	1.65	1.75	1.75	2	2	2	2.75
	Lactose	44	44	44	44	44	44	44	42
	Ethyl Cellulose	50	50	50	50	50	49.75	49.75	50
6	Aspartame	2	2	2	2	2	2	2	2
7	Talc	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75
8	Magnesium Stearate	QS	-	-	-	-	-	-	-
9.	Water	QS	-	-	-	-	-	-	-
10	Total Weight	400	400	400	400	400	400	405	406

Evaluation Parameters:

Table.7 Evaluation Parameters of Aminophylline Anhydrous Tablet

F. Code	Thickness (mm)±SD	Hardness (Kg/cm2)±SD	Friability (%)±SD	Weight Variation (mg)±SD	Drug Content Uniformity %
1	3.02±0.03	5.2±0.21	0.60±0.08	401±0.28	98.45
2	3.01±0.04	4.2±0.21	0.49±0.07	399±0.91	96.98
3	3.05±0.06	4.1±0.34	0.51±0.06	400±0.65	94.78

4	3.15±0.05	5.1±0.12	0.51±0.08	402±0.15	97.10
5	3.04±0.03	4.1±0.13	0.56±0.05	400±0.75	96.87
6	3.01±0.02	5.5±0.15	0.59±0.08	398±0.20	97.56
7	3.04±0.03	5.4±0.21	0.52±0.09	400±0.31	98.90
8	3.01±0.02	5.3±0.20	0.62±0.10	399±0.58	99.10

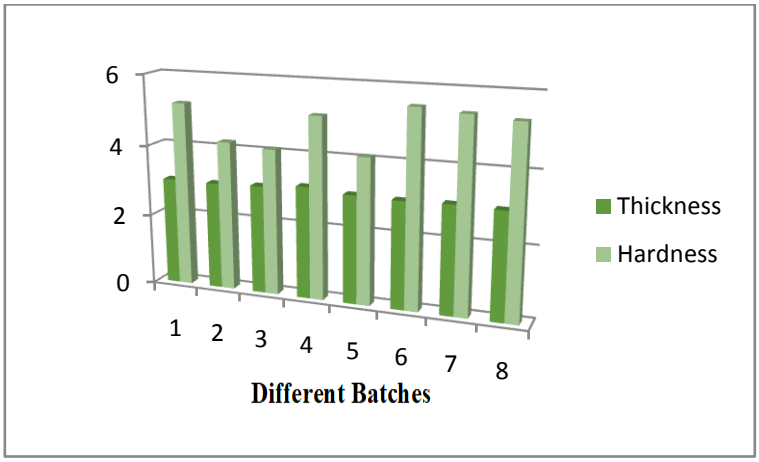

Fig.8 A Diagrammatically Representation of Hardness and Thickness

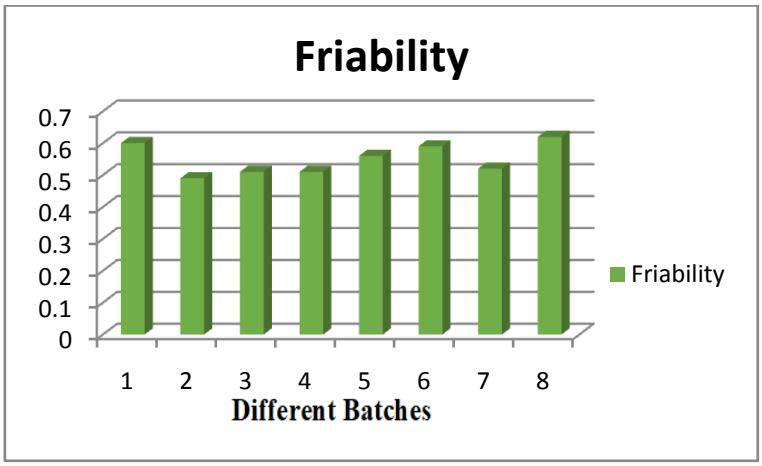

Fig.9 A Diagrammatically Representation of Friability

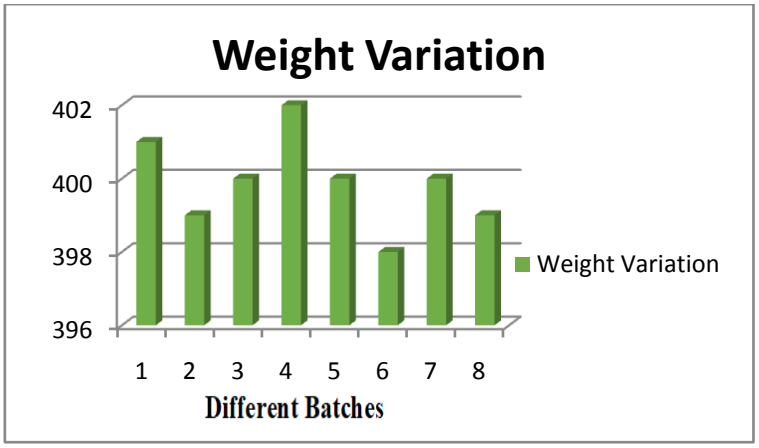

Fig.10 A Diagrammatically Representation of Weight Variation

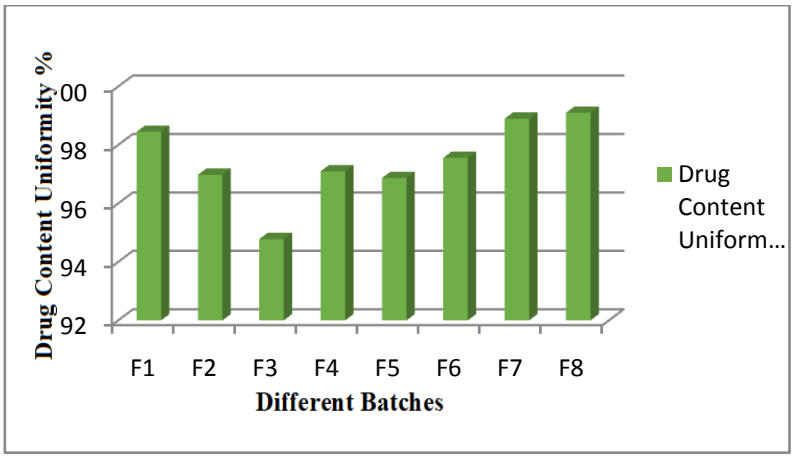

Fig.11 A Diagrammatically Representation of % Drug Content

In *vitro* Dissolution Profile

Table.8 In-Vitro Dissolution Study

Time (hr)	F1	F2	F3	F4	F5	F6	F7	F8
1	25.64±0.1	24.21±1	26.01±0.2	28.45±1.3	29.24±1.5	30.24±0.8	32.14±1.5	30.02±0.5
2	32.12±0.3	27.47±1.2	28.14±0.4	29.12±1.4	34.25±0.3	35.01±0.7	36.25±1.5	40.22±0.89
4	39.21±0.4	33.65±1.2	33.85±0.8	30.14±1.3	33.45±0.8	34.24±1.4	35.85±1.5	51.12±0.4
6	48.25±1	42.20±1.7	43.25±1.2	36.14±1.8	37.85±0.7	39.12±1.7	40.12±1.9	62.14±0.7
8	55.54±0.1	49.32±1.2	51.24±1.4	42.12±1.6	42.89±0.9	43.12±1.7	44.25±1.5	76.89±0.4
10	68.21±0.8	59.32±1.5	61.14±1.8	55.65±1.3	56.78±0.7	58.24±1.3	59.89±1.6	89.25±0.8
12	75.32±0.7	71.52±1.7	75.21±1.7	68.12±1.9	76.17±0.5	76.78±1.2	80.24±1.7	94.25±0.9

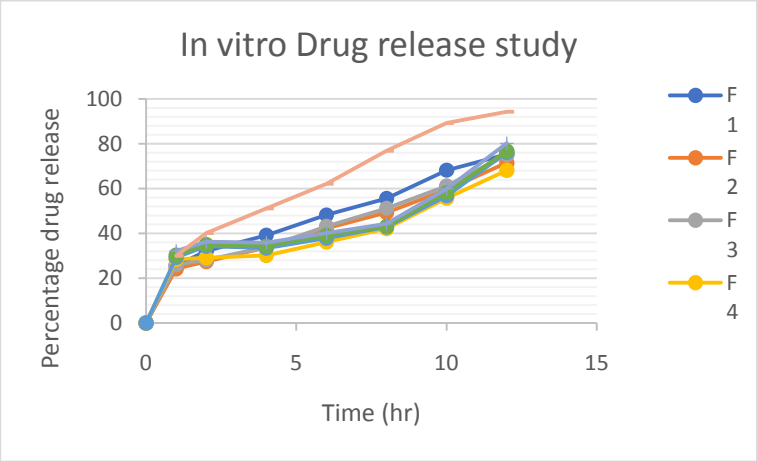

Fig.13 In vitro Drug release study

Discussion:

From the above vitro dissolution chart and study it was conclude that the formulation F8 is found the batter drug release up to 12hrs due change in concentration of polymer in the previous formulation chart. The formulation F8 is give the maximum drug release upto 94.25±0.9.

Kinetic Parameters of all Formulations:

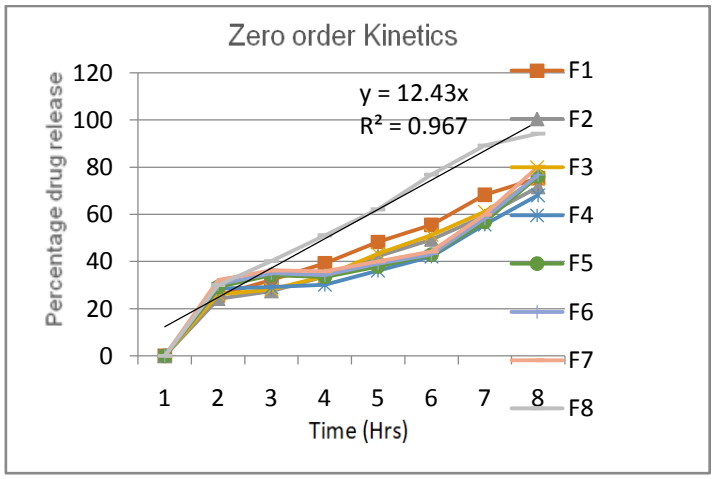

Fig.14 Zero Order Kinetics

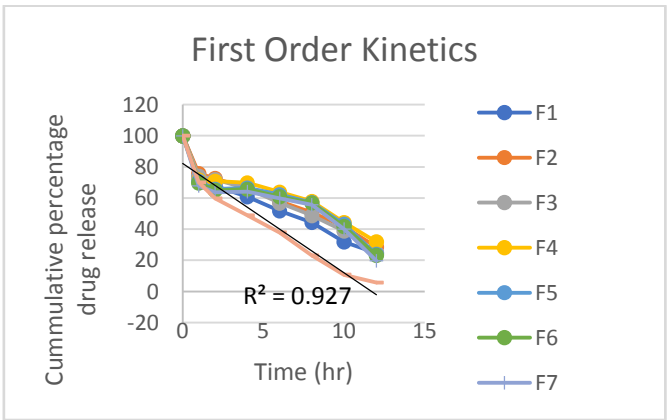

Fig.15 1st Order Kinetics

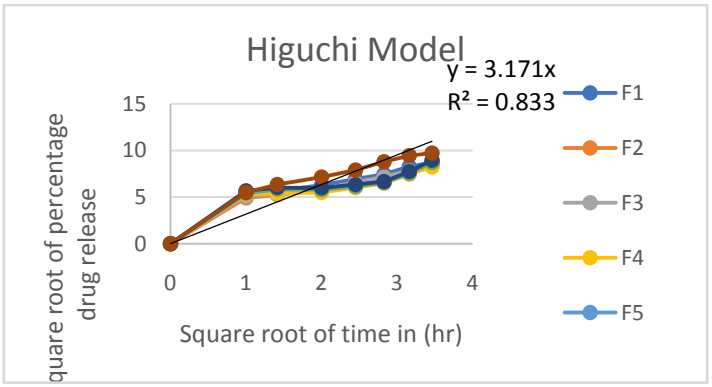

Fig.16 Higuchi Model

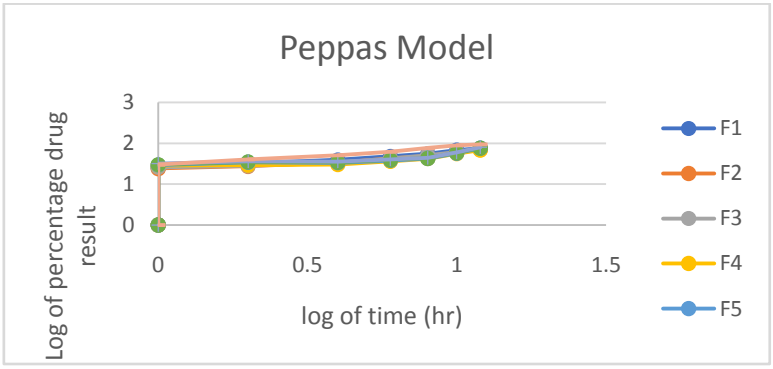

Fig.17 Peppas Model

Table.9 Release kinetic for the Optimized Formulations

Formulation	0-Order	1st-Order	Higuchi Model	Peppas Model
	R^2	R^2	R^2	R^2
1	0.950	0.923	0.892	0.545
2	0.942	0.926	0.878	0.691
3	0800	0.925	0.890	0.542
4	0.757	0.817	0.826	0.485
5	0.808	0.843	0.812	0.476
6	0.800	0.827	0.806	0.471
7	0.784	0.817	0.799	0.463
8	0.971	0.927	0.833	0.552

The kinetic property was necessary to find out the nature of the formulated tablet. In *vitro* drug release data of (F8) were fitted into various kinetics models.

Stability Studied:

Table.10 Stability study for best formulation F8

S. No.	Parameters	Initial	1 Month	2Month	3Month
1	Colour	White	No Change	No Change	No Change
2	Hardness	3.0±0.34	3.0±0.30	3.0±0.28	3.0±0.1
3	Friability	0.48±0.10	0.48±0.10	0.50±0.11	0.51±0.12
4	In-Vitro Drug Release	94.25±0.9	94.25±0.0.9	94±0.0.21	94.0±0.1

Discussion:

The duration of stability studies of the Formulation 8, there is no major variation in colour, the minor variation found in hardness, Friability and In vitro drug release that is adjustable, All data evaluated according to ICH guidelines at 40±2°C/75±5% RH for 90 days.

Summary

The formulation of the oral bio-adhesive Aminophylline Anhydrous tablet, various hydrophilic polymers and their combinations were used in varying concentrations of mucoadhesive polymer like HPMC K4M, Carbopol 934, Ethyl Cellulose, Aspartame, Talc and Magnesium Stearate added to the formulation are essentially required to achieve in-vitro buoyancy, desirable drug release, and excellent bioadhesive strength. Tablets were subject to various evaluation parameters such as Hardness, Friability, Drug content, Weight Variation and in vitro drug release study. It was revealed that tablets of all batches had acceptable physical parameters. After scanning of the sample drug, the wave length is obtained about 274nm in pH 7.2 phosphate buffers by using UV Spectroscopy Method Fig 6.1. Aminophylline Anhydrous showed maximum absorbance in phosphate buffer pH 7.2 at 274nm. The solution obeyed Beer-Lambert's law for concentration range of 0 to 30µg/ml with regression coefficient of 0.949. Standard curve of theophylline prepared in phosphate buffer pH 7.2 is shown in fig.5.1. Dry sample of drug and potassium bromide was mixed uniformly and filled into the die cavity of sample holder and an IR spectrum was recorded using diffuse reflectance FTIR spectrophotometer (Shimadzu FTIR 84005). The results of IR spectra obtained were revealed by figures 03-06. The results depicted that all characteristic peaks of Aminophylline Anhydrous with HPMC K4M, Carbopol-940, Ethyl cellulose and physical mixture of formulation within the range of pure Aminophylline Anhydrous revealing lack of significant interaction between drug and selected polymers for formulation of press coated tablets. From the above vitro dissolution chart and study it was conclude that the formulation F8 is found the batter drug release up to 12hrs due change in concentration of polymer in the previous formulation chart. The formulation F8 is give the maximum drug release upto 94.25±0.9. The kinetic property was necessary to find out the nature of the formulated tablet. In *vitro* drug release data of (F8) were fitted into various kinetics models. The duration of stability studies of the Formulation 8, there is no major variation in colour, the minor

variation found in hardness, Friability and In vitro drug release that is adjustable, All data evaluated according to ICH guidelines at 40±2°C/75±5% RH for 90 days. Tablets of batch F8 have good mucoadhesion along with in vitro drug release. It was observed that tablets of all batches followed the equation of Zero, 1st Order Release Kinetics, Korsmeyer and Peppas drug release profiles. Tablets of Batch F8 were selected as an optimum batch. Stability studies revealed that there was no significant change in the hardness, friability, drug content, and dissolution profile of formulation F8. Thus, this formulation was stable at different conditions of temperature. The present study shows that can be used for designing a mucoadhesive CR drug delivery system. Various hydrophilic polymers and their combinations were used in varying concentrations of mucoadhesive polymer like HPMC K4M, Carbopol 934, Hence it may increase the therapeutic efficacy of the drug by increasing the bioavailability and patient compliance and stimulates the skeletal muscles.

Conclusion:

The formulation of the oral bioadhesive Aminophylline Anhydrous tablet, various hydrophilic polymers and their combinations were used in varying concentrations of mucoadhesive polymer like HPMC K4M, Carbopol 934, Ethyl Cellulose, Aspartame, Talc and Magnesium Stearate added to the formulation are essentially required to achieve in-vitro buoyancy, desirable drug release, and excellent bioadhesive strength. Tablets were subject to various evaluation parameters such as Hardness, Friability, Drug content, Weight Variation and in vitro drug release study. It was revealed that tablets of all batches had acceptable physical parameters. Tablets of batch F8 have good mucoadhesion along with in vitro drug release. It was observed that tablets of all batches followed the equation of Zero, 1st Order Release Kinetics, Korsmeyer and Peppas drug release profiles. Tablets of Batch F8 were selected as an optimum batch. Stability studies revealed that there was no significant change in the hardness, friability, drug content, and dissolution profile of formulation F8. Thus, this formulation was stable at different conditions of temperature. The present study shows that can be used for designing a mucoadhesive CR drug delivery system. Various hydrophilic polymers and their combinations were used in varying concentrations of mucoadhesive polymer like HPMC K4M, Carbopol 934, Hence it may increase the therapeutic efficacy of the drug by increasing the bioavailability and patient compliance and stimulates the skeletal muscles.

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