ejpmr, 2017,4(9), 621-628

SJIF Impact Factor 4.161

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

FORMULATION AND OPTIMISATION OF CONTROLLED RELEASE TABLETS OF AMBROXIL HYROCHLORIDE TABLETS

A. Rajesh*[1] and K. Swapna[2]

[1]Hindu College of Pharmacy, Guntur -522 002.
[2]MLR Institute of Pharmacy, Hyderabad-500 043.

***Corresponding Author: Dr. A. Rajesh**
Hindu College of Pharmacy, Guntur -522 002.

Article Received on 11/07/2017 **Article Revised on 31/07/2017** **Article Accepted on 21/08/2017**

ABSTRACT

In the present work, an attempt has been made to prepare controlled release matrix tablets of ambroxol hydrochloride, a mucolytic expectorant by wet granulation method using xanthan gum as natural hydrophilic polymer in three different ratios (Drug : Polymer 1:1,1:1.5, 1:2) .The prepared granules of three different formulations were evaluated for angle of repose, loose bulk density (LBD), tapped bulk density (TBD) and compressibility index(CI), hausners ratio and This was further supported by lower compressibility index values. Generally CI values up to 15% results in good to excellent flow properties. the percentage porosity values of the granules ranged from 26.92% - 34.52%, indicating that the packing of the granules may range from close to loose packing and also conforming that the particles are not of greatly different sizes. The prepared tablets were tested for physical parameters like weight variation, hardness, friability, content of active ingredient and In-vitro drug release studies. The percent deviation is with in the prescribed official limits.

KEYWORDS: In the present work, with in the prescribed official limits.

INTRODUCTION

Controlled release drug delivery systems are designed by different techniques like enteric coating, osmotic pump, prodrugs, transdermal patches and matrix tablets. Among the various techniques used, recently the attention of pharmaceutical researchers has been attracted by the matrix tablets because of their ease of manufacturing. Different types of polymers are used to control the release of drugs from the dosage forms for absorption by the body. Though a variety of polymeric substances are available to serve as release retarding matrix materials there is a continued need to develop new, safe and effective release retarding materials for matrix tablets. Natural gums and poly saccharides and their derivatives represent a group of polymers widely used in pharmaceutical dosage forms due to their non-toxicity, low cost and free availability. Natural gums and hydrophilic polymers and where in contact with water, their hydrated to form a gel. Because of this property natural gums like gum karaya, Xanthan gum, and olibanun gum have been reported as good matrix materials for sustained release dosage forms.[1]

This is compatible with variety of active ingredients and other excipients and readily hydrate, absorb water and swell quickly. Because of their hydrophilic nature, and highly cross-linked structure they are more suitable candidates for use in controlled release drug delivery systems. Ambroxol is a metabolite of bromhexine with similar action and uses. It is chemically described as trans-4[(2-amino -3, 5-dibromo benzyl] amino]-cyclohexanol. It has been successfully used for decades in the form of its hydrochloride as a secretion –releasing expectorant in a variety of respiratory disorders. It's short biological half life (4hr) that calls for frequently daily dosing (2 to 3 times) and therapeutic use in chronic respiratory diseases necessitates its formulation in to sustained release dosage form. The objective of the present study was to formulate Ambroxol hydrochloride SR matrix tablets using guar gum (natural polymer) and to elucidate the release kinetics of Ambroxol hydrochloride from guar gum –matrices. Here, an attempt was made by a systematic approach to develop twice-daily sustained release Ambroxol hydrochloride matrix tablets.[2]

MATERIALS AND METHODS

Materials: Ambroxol hydrochloride was generously supplied as a gift sampleby Alembic Ltd. Vadodara, India. Xanthum gum was obtained from Essex, UK, Starch and Magnesium from Sigma Aldrich, Germany.

Methods[3]

Standard plot of Ambroxol hydrochloride with 0.1N HCL

10 mg of Ambroxol hydrochloride was dissolved in 0.1N HCL and make up the volume upto 100 ml, and further dilutions were made using 0.1N HCL .The absorbance of

the solutions were measured at 248nm using ELICO UV-Visible spectrophotometer. The experiment was repeated in triplicate and the average of three readings was taken to plot the standard curve.

Standard plot of Ambroxol hydrochloride with pH 6.8

10 mg Ambroxol hydrochloride was dissolved in. pH 7.4 buffer and make up the volume upto 100 ml and further dilutions were made using pH 7.4 buffer to obtain concentration ranging from 5µg/ml to 40µg/ml. The absorbance of the solutions were measured at 248nm using ELICO UV- Visible spectrophotometer. The experiment was repeated in triplicate and the average of three readings was taken to plot the standard curve.

Granulation Properties

The methods to measure certain granulation characteristics have been developed to monitor granulation suitability for tableting. Good flow properties are essential for the transport of the material through the hopper into and through the feed frame and in to dies.

Angle of repose

The frictional force in a loose powder can be measured by the angle of repose θ. It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides of the pile until the mutual friction of the particles producing a surface angle θ, is in equilibrium with the gravitational force. The angle of repose was determined by the funnel method suggested by Newman. The blend was poured through a funnel that can be raised vertically untill a maximum cone height (h) was obtained. Radius of the heap (r) was measured and the angle repose was calculated using the following formula,

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

Therefore $\theta = \tan^{-1} (h/r)$

Bulk Density

Density is defined as weight per unit volume. Bulk density, P_b, is defined as the mass of the powder divided by the bulk volume and is expressed as gm/ cm^3. The bulk density of a powder primarily depends on particle size distribution, `particle shape and the tendency of particles to adhere together. There are two types of bulk density.

Apparent bulk density (Pb) was determined by pouring blend into a graduated cylinder. The bulk volume (Vb) and weight of the powder (M) was determined. The bulk density was calculated by using the following formula

$$Pb = M/Vb$$

Where,

P_b = Bulk Density"
M = Weight of sample in gm
Vb = Final volume of blend in cm^3

Tapped Density

It is the ratio of total mass of the powder to the tapped volume of powder. The volume was measured by tapping the powder for 500 times. Then the tapping was done for 750 times and the tapped volume was noted. The tapped density was calculated by using the following formul

$$Pt = M/Vt$$

Where,

Pt = Tapped Density
M = Weight of the sample in gm
Vt = tapped volume of blend in cm^3

Compressibility Index and Hausners ratio[4]

In recent years, the compressibility index and the closely related Hausner ratio have become the simple, fast, and popular methods of predicting powder flow characteristics. The compressibility index has been proposed as an indirect measure of bulk density, size and shape, surface area, moisture content and cohesiveness of materials, because all of these can influence the observed compressibility index. The compressibility index and the Hausner ratio are determined by measuring both the bulk volume and tapped volume of a powder.

Basic methods for the determination of compressibility Index and Hausner Ratio

While there are some variations in the method of determining the compressibility index and Hausner ratio, the basic procedure is to measure the unsettled apparent volume, (V_0) and the final tapped volume, (V_f), of the powder after tapping the material until no further volume changes occur. The compressibility index and the Hausner ratio are calculated as follows:

$$Compressibility\ Index = 100 \times \frac{V_0 - V_f}{V_0}$$

$$Hausner\ Ratio = \frac{V_0}{V_f}$$

Alternatively, the compressibility index and Hausner ratio may be calculated using measured values of bulk density and tapped density as follows:

Compressibility Index = 100 × Tapped density / Bulk density

Hausner Ratio = Tapped density/ Bulk density

Preparation of Matrix Tablets

Matrix tablets of Ambroxol hydrochloride using xanthamgum in different proportions were prepared by wet granulation method using 1:1 ratio of methanol and water mixture microcrystalline cellulose (MCC) was used as diluent. The composition of different formulations used in the study is given in table. The required quantities of medicaments and matrix materials were mixed thoroughly in a mortar by following geometric dilution technique. The 1:1 ratio of methanol and water mixture was added and mixed thoroughly to form a dough mass. The mass was passed through a mess no.14 to obtain wet granules. The wet granules were dried at 50º for 30 min. The dried granules were passed

through mess no.14 to break the aggregates. These granules were lubricated with a mixture of talc and magnesium stearate (2:1). The lubricated granules were compressed in to tablets on a rotary multi-station tableting machine with required hardness using 9 mm round and flat punches.

Table. 1: Formula for formulation of matrix tablets

S.NO	INGREDIENTS	F1 (1:1)	F2 (1:1.5)	F3 (1:2)
1.	Ambroxol hcl	75mg	75mg	75mg
2.	Xantham gum	75mg	112mg	150mg
3.	Microcrystalline cellulose	80mg	43mg	5mg
4.	Starch	12.5mg	12.5mg	12.5mg
5.	Talc	5.0mg	5.0mg	5.0mg
6.	Magnesium stearate	2.5mg	2.5mg	2.5mg
	Total Weight	250mg	250mg	250mg

Evaluation of Tablets[5-9]

The prepared matrix tablets were evaluated for General appearance, thickness, hardness, weight variation, friability and drug content.

General appearance

The tablets prepared were white, round, spherical shape. They were smooth, uniform and free from cracking and chipping.

Thickness and diameter

The thickness and diameter of the tablets were determined by Vernier caliper. Three tablets from each batch were used and the average values were calculated.

Hardness test

Hardness (diametral crushing strength) is a force required to break a tablet across the diameter. The hardness of a tablet is an indication of its strength. The tablet should be stable to mechanical stress during handling and transportation. The degree of hardness varies with the different manufactures and with the different types of tablets. The force is measured in kilograms. The hardness was tested using Monsanto tester. "Hardness factor", the average of the five determinations, was determined and reported.

Uniformity of weight (Weight variation test)

This is an important in-process quality control test to be checked frequently (every half an hour). Corrections were made during the compression of tablets. Any variation in the weight of tablet (for any reason) leads to either under medication or overdose. So, every tablet in each batch should have a uniform weight. 20 tablets were weighed individually. Average weight was calculated from the total weight of all tablets. The individual weights were compared with the average weight. The percentage difference in the weight variation should be within the permissible limits (± 5%). The percent deviation was calculated using the following formula.

$$\% \text{ Deviation} = \frac{\text{Individual weight} - \text{Average weight}}{\text{Average weight}} \times 100$$

Friability test

Friability is the loss of weight of tablet in the container/package, due to removal of fine particles from the surface. This in-process quality control test is performed to ensure the ability of tablets to withstand the shocks during processing, handling, transportation and shipment. Roche friabilator was used to measure the friability of the tablets. It was rotated at a rate of 25 rpm. Ten tablets were weighed collectively and placed in the chamber of the friabilator. In the friabilator, the tablets were exposed to rolling, resulting from free fall of tablets within the chamber of the friabilator. After 100 rotations (4 minutes), the tablets were taken out from the friabilator and intact tablets were again weighed collectively. Permitted friability limit is 1.0%. The percent friability was determined using the following formula.

$$(W_1 - W_2)/W_1 \times 100$$

Where,

W_1 = weight of the tablet before test

W_2 = weight of the tablets after test

Content of active ingredient

To ensure the consistency of dosage units, each unit in a batch should have active substance content within a narrow range around the label claim. Dosage units are defined as dosage forms containing a single dose or a part of a dose of an active substance in each dosage unit. The term "Uniformity of dosage unit" is defined as the degree of uniformity for substance among dosage units. The test for content uniformity is based on the assay of the active medicament of content uniformity is necessary the quantity of the active medicament is within the limit in the formulation. Ten tablets from each formulation were powdered. The powder equivalent to 100 mg of theophylline was weighed and dissolved in phosphate buffer pH 6.8 in 100 ml standard flask. From this 10 µg/ml, equivalent solution was prepared and analyzed at 244 nm using UV spectrophotometer. Generally, the drug content in any formulation should fall within the limit of 90 – 110%.

Drug-Excipient Compatibility Studies

Fourier Transform Infrared Spectroscopy

Infrared spectra matching approach was used for the detection of any possible chemical reaction between the drug and the polymer. A physical mixture (1:1) of drug and polymer was prepared and mixed with suitable quanta of potassium bromide. About 100 mg of this mixture was compressed to from a transparent pellet using a hydraulic press at 10 tons pressure. It was scanned from 4000 to 400 cm^{-1} in a shimadzu FTIR 8400 Spectrophotometer. The IR spectrum of the physical mixture was done to detect any appearance or disappearance of peaks. The compatibility between the drug and the polymer were evaluated using FTIR matching method.

***In vitro* drug release studies**

In vitro drug release studies were carried out using USP XXIV dissolution apparatus type II, with 900ml of dissolution medium maintained at 37±1° for 12 h, at 100 rpm, 0.1 N HCL was used as a dissolution medium for first 2h followed by pH 6.8 ± 0.2 phosphate buffer for further 10 h. 10ml of sample was withdrawn at predetermined time intervals replacing with an equal quantity of drug free dissolution fluid. The samples withdrawn were filtered through 0.45µ membrane filter, and drug content in each sample was analyzed after suitable dilution by UV/Vis Spectrophotometer at 244 nm, and cumulative percent drug release was calculated. The study was performed in triplicate. The commercial Ambroxol SR tablets were used as the reference formulation and were also subjected to Invitro drug release studies so as to choose the optimal amount of guar gum in the matrix tablets.

Dissolution studies

In- vitro drug release studies details.

Apparatus used : USPII dissolution test apparatus
Dissolution medium : pH6.8 and 0.1N hcl
Dissolution medium volume : 900 ml
Temperature : 37 + 0.5 ^{0}C
Speed of paddle : 50 rpm
Sampling intervals : 30 min up to 2 hours, 1 hour up to 10 hours
Sample volume : 10ml
Absorption measurement : 244nm

Drug release kinetics-model fitting of the dissolution Data

Whenever a new solid dosage form is developed or produces, it is necessary to ensure that drug dissolution occurs in an appropriate manner. The pharmaceutical industry and the registration authorities do focus, nowadays, on drug dissolution studies. Drug dissolution from solid dosage forms has been described by kinetic models in which the dissolved amount of drug (Q) is a function of the test time, t or Q = f(t) **.** Some analytical definitions of the Q (t) function are commonly used, such as zero order, first order Hixson-crowell, weibull, higuchi, korsmeyer –peppas models. Other release parameters, such as dissolution time ($t_{x\%}$), dissolution efficacy (ED), difference factor (f_1), similarity factor (f_2) can be used to characterize drug dissolution / release profile.

1. zero-order kinetics: A zero-order release would be predicted by the following equation.

$$\mathbf{At = A_o - K_o t} \quad \text{…… 1}$$

Where
At = drug release at time t
A_o = initial drug concentration
K_o = zero-order rate constant (hr)

When the data is plotted as cumulative percent drug release versus time, if the plot is linear then the data obeys zero-order release kinetics, with a slope equal to k_o.

Use

This relation can be used to describe the drug dissolution of several types of modified release pharmaceuticaldosage forms, as in case of some transdermal systems etc. the pharmaceutical dosage forms following this profile release the same amount of drug by unit of time and it is the ideal method of drug release in order to achieve a prolonged pharmacological action.

First-order kinetics

A first order release would be predicted by the following equation.

$$\mathbf{Log\ C = Log\ Co - Kt / 2.303} \quad \text{…….. 2}$$

Where
C = amount of drug remained at time t
Co = initial amount of drug
K = first-order rate constant

When the data is plotted as log cumulative percent drug remaining versus time yields a straight line indicating the release follows first-order kinetics, the constant k can be obtained by multiplying 2.303 with slope values.

Use: The pharmaceutical dosage forms containing water-soluble drugs in porous matrices, follows this type of dissolution profile. The release of the drug is proportional to the amount of drug remaining in its interior so that the amount of drug release by unit of time dimnishes.

Higuchi model

Drug release from the matrix devices by diffusion has been described by following higuchis classical diffusion equation.

$$\mathbf{Q = [DE/ \tau(2A- ECs)\ C_{st}\ ]} \quad \text{…… 3}$$

Where
Q = amount of drug release at time t

D = diffusion coefficient of the drug in the matrix
A = total amount of drug in unit volume of matrix
C_s = the solubility of the drug in the matrix
E = porosity of the matrix
T = time in hrs at which q is the amount of drug is release

Equation-3 may be simplified if one assumes that D, Cs and A are constant. Then equation-3 becomes

Q = K t ½

When the data is plotted according to equation- 4 i.e cumulative drug release versus square root of time, yields a straight line, indicating that the drug was released by diffusion mechanism. The slope is equal to k.

Use

The relation can be used to describe the drug dissolutionfrom several types of modified release pharmaceutical dosage forms, as in case of some water soluble drugs.

Korsmeyer model

In order to understand the mode of release of drug from swellable matrices, the data were fitted to the following Peppa's law equation

$\mathbf{M_t / M_{\acute{a}} = Kt^n}$

Where,

$M_t / M_{\acute{a}}$ = The fraction of drug released at time't'.

K = Constant incorporating the structural and geometrical Characteristics of the drug / polymer system.
n = Diffusion exponent related to the mechanism of release.

The above equation can be simplified by applying log on both sides we get

$\mathbf{Log\ M_t / M_{\acute{a}} = Log\ K + n\ Log\ t}$

When the data is plotted as a log of drug released versus log time, yields a straight line with a slope equal to n and the k can be obtained from y- intercept.

The value of n for a cylinder is <0.45 for fickian release, > 0.45 and < 0.89 for non-fickian release, 0.89 for the case 2 release and > 0.89 for super case2 type release.

Short-term stability studies

Short term stability studies was performed at 45oC over a period of three weeks on the matrix tablet formulation(F3) sufficient number of tablets (10) were packed in amber-coloured screw capped bottles and kept in ovens maintained at 450c. samples were taken at weekly intervals for a drug content estimation shown in table. At the end of three weeks period, dissolution test was performed to determine the drug release profiles. The data of dissolution after stability studies was shown in the table.

RESULTS AND DISCUSSION

Table-2 In-Vitro Drug Release Profile of Ambroxol hydrochloride Matrix Tablets.

S.no	Time (hrs)	Cumulative Percentage Drug Release			
		F -1	F - 2	F - 3	A - MS
1.	00.30	23.14 ± 0.43	21.33 ± 0.48	17.46 ± 0.60	15.86 ± 0.20
2.	01.00	26.54 ± 0.35	28.33 ± 0.20	25.50 ± 0.35	26.10 ± 0.45
3.	01.30	35.60 ± 0.20	34.53 ± 0.35	31.27 ± 0.35	28.15 ± 0.31
4.	02.00	40.01 ± 0.56	40.24 ± 0.35	35.50 ± 0.54	33.24 ± 0.24
5.	03.00	42.72 ± 0.35	41.45 ± 0.31	39.50 ± 0.30	40.09 ± 0.07
6.	04.00	48.93 ± 0.31	48.09 ± 0.17	46.41 ± 0.02	46.11 ± 0.41
7.	05.00	57.22 ± 0.31	53.69 ± 0.31	52.15 ± 0.32	51.78 ± 0.22
8.	06.00	61.96 ± 0.29	60.66 ± 0.18	59.60 ± 0.32	58.99 ± 0.51
9.	07.00	68.20 ± 0.36	66.64 ± 0.36	65.25 ± 0.26	65.28 ± 0.32
10	08.00	74.39 ± 0.31	72.82 ± 0.32	70.92 ± 0.52	71.25 ± 0.01
11	09.00	80.67 ± 0.31	78.46 ± 0.03	76.49 ± 0.46	77.50 ± 0.25
12	10.00	86.96 ± 0.31	85.48 ± 0.46	83.08 ± 0.47	84.13 ± 0.36
13	11.00	92.62 ± 0.30	91.95 ± 0.04	89.13 ± 0.27	89.18 ± 0.54
14	12.00	99.23 ± 0.27	98.35 ± 0.19	97.02 ± 0.31	97.30 ± 0.03

*A-MS: Ambroxol Marketed Sample.
*All the values are expressed as mean SE, n=3.

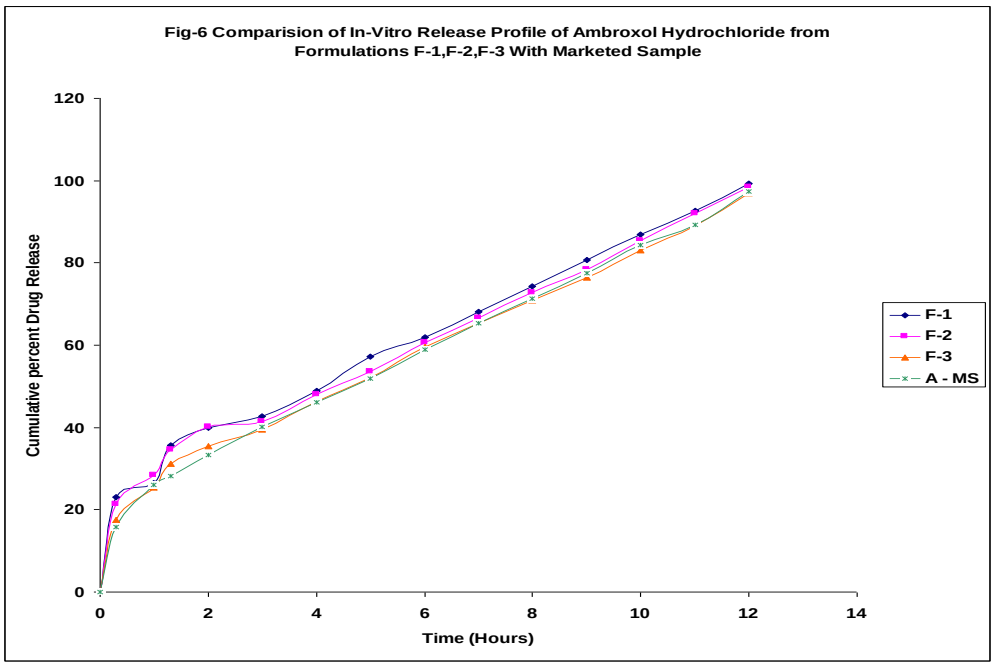

Fig: 1 Invitro drug release profile.

Table: 3 Drug release kinetics of Formulations.

Formulation code	Correlation Coefficient (r) Value			Korsmeyers – Peppas Plot	
	Zero order	First order	Higuchi equation	Slope (n)	Correlation Co-efficient
F – 1	0.9540	0.7442	0.9727	0.501	0.7419
F – 2	0.9950	0.7864	0.9686	0.523	0.7386
F – 3	0.9661	0.8302	0.9760	0.701	0.7205
A – MS	0.9718	0.8443	0.9796	0.706	0.5034

*****A-MS : Ambroxol hydrochloride Marketed Sample.

Table-4 stability data for Formulation F-3 at 45 ±1ºc.

S.NO	Time in days	Physical changes	percentage drug content
1.	00	----	99.40 ± 0.92
2.	15	No change	99.30 ± 0.97
3.	30	No change	99.10 ± 0.98
4.	45	No change	99.06 ± 0.90

*****All the values are expressed as mean, S.E n=3.

Table-5 In-vitro Release Profile for Stability Formulation F-3.

S.NO	Time (hrs)	Cumulative Percentage of Drug Release	
		1st day	45th day
1.	00.30	17.46 ± 0.60	16.80 ± 0.59
2.	01.00	25.50 ± 0.35	25.20 ± 0.38
3.	01.30	31.27 ± 0.35	30.91 ± 0.41
4.	02.00	35.50 ± 0.54	32.62 ± 0.36
5.	03.00	39.50 ± 0.30	39.81 ± 0.19
6.	04.00	46.41 ± 0.02	46.44 ± 0.35
7.	05.00	52.15 ± 0.32	51.78 ± 0.14
8.	06.00	59.60 ± 0.32	59.29 ± 0.46
9.	07.00	65.25 ± 0.26	65.28 ± 0.42
10.	08.00	70.92 ± 0.52	70.32 ± 0.38
11.	09.00	76.49 ± 0.46	76.29 ± 0.40
12.	10.00	83.08 ± 0.47	82.56 ± 0.36
13.	11.00	89.13 ± 0.27	89.06 ± 0.06
14.	12.00	97.02 ± 0.31	96.96 ± 0.03

In the present work, an attempt has been made to prepare controlled relese matrix tablets of ambroxol hydrochloride, a mucolytic expectorant by wet granulation method using xanthan gum as natural hydrophilic polymer in three different ratios (Drug: Polymer 1:1,1:1.5, 1:2). The prepared granules of three different formulations were evaluated for angle of repose, loose bulk density (LBD), tapped bulk density (TBD) and compressibility index(CI), hausners ratio and This was further supported by lower compressibility index values Generally CI values up to 15% results in good to excellent flow properties. the percentage porosity values of the granules ranged from 26.92% - 34.52%, indicating that the packing of the granules may range from close to loose packing and also conforming that the particles are not of greatly different sizes. The prepared tablets were tested for physical parameters like weight variation, hardness, friability, content of active ingredient and In-vitro drug release studies. The percent deviation is with in the prescribed official limits.

The IR spectrum shows that both drug and polymer were not interacted each other and appear as separate entities which is clearly shown in the spectra Both hydroxyl and secondary amino group stretching vibration were merged to each other and therefore appear on single strong broad band at 34229 cm^{-1} for Ambroxol pure drug, but in case of drug + polymer, hydroxyls of xantham gum and ambroxol and secondary amino of ambroxol to vibration were merged to each other and appear as a single broad hydrogen bonded band at 3404 cm^{-1}. All other stretching and bending vibration of standard drug was unaffected. Therefore from the above observations, both the standard and polymers are compatible and are not interacted each other.

The release of ambroxol from the matrix tablets was sustained up to 12hrs. The cumulative percentage of drug release was decrease with increase in polymer concentration. Among the three formulations F-3 gave the release profile close to the commercially available marketed sample of Ambroxol Hydrochloride(A-MS).

The release of drug depends not only on the nature of matrix but also upon the drug polymer ratio. As the percentage of polymer increased the kinetics of release decrease. This may be due to structural re organization of hydrophilic xanthan gum polymer. Increase in concentration of Xanthan gum may result in increase in the Tortuosity or gel strength of the polymer. Failure to generate a uniform and coherent gel may cause rapid drug release. The release data of matrix tablets were filled into various mathematical models (Zero order, First order, Higuchi's equation and Peppas equation) to evaluate the kinetics and mechanism of drug release from the tablets. The model that best fits the release data is selected based on the correlation co-efficient(r) value in various models. The model that gives high "r" value is considered as the best fit of the release data. The "r" values in zero, first-order and Higuchi models are given in Table. The results given in Table indicate indicated that the drug release from the matrix tablets followed Zero order kinetics. The regression co-efficient values (r^2) increases gradually with increase in polymer concentration. Release of the drug from a matrix tablet containing hydrophilic polymers generally involves factors of diffusion. To evaluate drug release mechanism from the tablets, plots of percent released vs. square root of time as per Higuchi's equation were constructed. All the formulations show better linearity for Higuchi release kinetics with (r2>0.97). It indicates that the drug release is by diffusion mechanism. The dissolution data was fitted to Korsmeyer equation which is used to describe the drug release behaviour from polymeric systems. Plots of Log cumulative percent drug release versus log time gives r2 values. The values of n<0.43 indicates Fickian release, >0.45 but <0.85 indicates Non-Fickian release. All the formulations showed diffusion co-efficient value (n) greater than 0.43 but less than 0.85 after fitting to the Korsmeyer equation as shown in the (Table-12). so, it indicates Non-Fickian transport mechanism. Therefore the drug release is by diffusion and erosion mechanism.

The stability studies were carried out for F-3 formulation at 45°C with 75% RH for 45 days revealed that no considerable differences in drug content and dissolution were observed.

CONCLUSION

From the present study, the following conclusions are drawn. Matrix tablets of Ambroxol Hydrochloride using xanthan gum prepared by wet granulation method were found to be good in appearance. The granules showed satisfactory flow properties and compressibility index. Quality control tests were performed for prepared tablets and they are with in the prescribed limits as per I.P specifications. The drug content was uniform in all the formulations of tablets prepared. The results indicate uniform distribution of drug with in the matrices.IR spectroscopic studies indicated that the drug is compatible with the polymer. The drug-polymer ratio was found to influence the release of drug from the formulations. As the polymer level is increased, the drug release rates was found to be decreased. Drug release was found to follow zero order kinetics and the mechanism of drug release was found to be diffusion and erosion. Formulation F-3 i.e(1:2 drug:polymer) exhibited the similar In-vitro drug release rates as that of the marketed sample. Short-term stability studies indicated that no appreciable changes in the drug content and In-vitro drug release rates of formulation F-3.

REFERENCES

1. Shangraw, R.F., Compressed tablets by direct compression. In: Liberman, H.A., Lacmann, L., Schwartz, J.B.(Eds), pharmaceutical dosage forms, Tablets Vol-1,2nd Edn., Marcel Dekker, Newyork, 1989; 195-243.

2. Aulton, E.m., Pharmaceutical technology, Pharmaceutics The Science of Dosage form design, 1990; 610-612.
3. The United States Pharmacopoeia, 1942. The United States Pharmacopoeial Convention, Rockville, MD: 1942.
4. Mulye, N.V., Turco, S.J.,. A simple model based on first order kinetics to explain release of highly water soluble drugs from porous dicalcium phosphate dehydrate matrices .Drug Dev Ind. Pharm. 1995; 21: 943-953.
5. Schwarz, B.J., Simonelli, A.P., Higuchi, W.I., .Drug release from wax matrices. I.
6. Analysis of data with first order Kinetics and with the diffusion controlled model. j. pharm. Sci., 1998; 57: 274-277.
7. Varelas, C.G Dixon, D.G., Steiner, C.,. Zero –order release from biphasic polymer hydrogels. J. Control. Release, 1995; 34: 185-192.
8. Colombo P, Bettini Release, Catellani PL, et al. Drug Volume Fraction Profile in the gel phase and drug release kinetics in hydroxyl propyl methyl cellulose matrices containing a soluble drug. Eur j Pharm Sci., 86: 323-328.
9. Kim, H., Fassihi, R..,. Application of binary polymer system in drug release rate modulation. 2. Influence of formulation variables and hydrodyanamic conditions on release kinetics. J. Pharm. Sci. 1997; 86: 323-328.