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Effect of gums and excipient on drug release and swelling of Ambroxol Hydrochloride Sustained Release Matrices

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ABSTRACT

Introduction: Matrices of Ambroxol hydrochloride with natural gums like Xanthan gum, Guar gum and κ-Carrageenan gum and their combinations at different ratios were done to develop a sustained release dosage form.Matrix tablets were formulated using natural gums like Xanthan gum, Guar gum and κ-Carrageenan gum and their combinations at different ratios. The effect of water-soluble and water insoluble excipients such as Lactose, Avicel 102 and Dicalcium phosphate on release profiles of gums and swelling in pH 6.8 phosphate buffer was studied and fitted to various release kinetics models. Accelerated stability studies were conducted as per ICH Guidelines at 40°C/75% RH for 6 months. Xanthan gum and κ-Carrageenan gum retarded the drug release more than Guar gum. Avicel 102 and Lactose enhanced the dissolution rate whereas Dicalcium phosphate retarded the drug release. It can be concluded that that utilization of natural gums is an effective system for obtaining sustained release of drugs.

Key Words: - Sustained release, gums, excipients, drug release, swelling.

INTRODUCTION

Ambroxol is a metabolite of bromhexine with similar actions and uses. It is chemically described as trans-4- [(2-Amino-3, 5-dibromobenzyl) amino]-cyclohexanol. It is an expectoration improver and a mucolytic agent used in the treatment of acute and chronic disorders characterized by the production of excess or thick mucous. It has been successfully used for decades in the form of its hydrochloride as a secretion-releasing expectorant in a variety of respiratory disorders. Its short biological half life (4 h) that calls for frequent daily dosing (2 to 3 times) and therapeutic use in chronic respiratory diseases necessitates its formulation into sustained release dosage form.

Generally, primary objectives of controlled drug delivery are to ensure safety and to improve efficacy of drugs as well as patient compliance, which can be achieved by better control of plasma drug levels and less frequent dosing.The most convenient way to achieve controlled release of active agent involves physical blending of drug with polymer matrix, followed by direct compression, compression molding, injection molding, extrusion, or solvent casting which results either in monolithic device or in swellable hydrogel matrix. For any controlled-release dosage form it is very important to use minimum number of excipients with minimum processing steps in order to reduce the tablet-to-tablet and batch-to-batch variations, hence direct compression is the most suitable and easily up-scalable technique. On contact with an aqueous medium, the hydrophilic polymer matrix gradually begins to hydrate from the periphery towards the centre forming a gelatinous swollen mass, which controls the diffusion of drug molecules through the polymeric material into the aqueous medium. Natural gums are among the most popular hydrophilic polymers because of their cost-effectiveness and regulatory acceptance. Guar gum is a natural nonionic polysaccharide derived from the seeds of Cyamopsis tetragonolobus (Family Leguminosae). In pharmaceuticals, G gum is used in soliddosage forms as a binder and disintegrant.Xanthan gum is another natural, biosynthetic, edible gum and an extracellular polysaccharide produced by the bacterium Xanthomonas campestris. Xanthan gum consists of glucose, mannose, and glucuronic acid14 and is used in different foods as thickener and stabilizer.Carrageenans are naturally occurring high molecular weight polysaccharides extracted from seaweeds and are made up of the repeating units of galactose and 3,6 anhydrogalactose.They consist of the sulfate esters of galactose and 3,6 anhydrogalactose joined by alternating α-1,3 and β-1,4 glycosidic linkages.There are 3 main types of carrageenans available: iota (ι), kappa (κ), and lambda (λ), with 1, 2, or 3 ester sulfate groups, respectively The objective of this study was to develop matrix sustained-release tablets of Ambroxol using natural gums (xanthan, guar and Carrageenan gum) as suitable hydrophilic matrix systems compared with the extensively investigated hydrophilic matrices (ie, hydroxypropyl methylcellulose [HPMC]/carboxymethyl cellulose [CMC] with respect to in vitro drug release rate and hydration rate of the polymers. [C.Sweetman et.al., H.Vergin et.al., J.R.Robinson et.al., H. Santos et.al., S.M. Al-Saidan et.al., G. Shlieout et.al., P.Colombo et.al., P.Colombo et.al., V.B.Pai et.al.,B.R. Mathews et.al., I.A. Castro et.al., N Errington et.al.]

MATERIALS AND METHODS

2.1 Materials:-

The drug Ambroxol Hydrochloride was procured as gift sample from (Shreya Pharmaceuticals Limited, Aurangabad,India),Xanthan gum, Guar Gum, κ-Carrageenan gum were procured from (Loba Chemicals,Munbai,India), Avicel PH 102.Dicalcium Phosphate and Lactose were procured from (Emcure Pharmaceuticals,Pune,India). All other chemicals were purchased and were of analytical grade.

2.2Preparation of Matrices:-[V. K. Guptaa et.al.]

Ambroxol hydrochloride, Xanthan gum, Guar gum and κ-carrageenan gum were mixed separately in various ratios individually and in combinations with each other in a laboratory mixer and were passed through 40-mesh screen. Lactose, Avicel102 and dicalcium phosphate were used as fillers-binders for the matrices. The formulations prepared are presented in Table No.01. The tablets were compressed by direct compression method by using 8 Station Tablet

Punching Machine – Karnavati - Minipress D-II Link, Mumbai fitted with 8-mmdiameter flat-faced punches. Powder admixtures were manually filled into the die, and 1 compaction cycle was performed. For each batch, 50 tablets were produced.

Table No.01:-Composition of 75 mg Ambroxol HCl Matrices (according to mg)

Batch No	Xanthan gum	Guar gum	Carrageenan gum	Lactose	Avicel 102	DCP
X1	75	--	--	--	--	--
X2	150	--	--	--	--	--
G1	--	75	--	--	--	--
G2	--	150	--	--	--	--
C1	--	--	75	--	--	--
C2	--	--	150	--	--	--
XG1	37.5	112.5	--	--	--	--
XG2	75	75	--	--	--	--
XG3	112.5	37.5	--	--	--	--
GC1	--	37.5	112.5	--	--	--
GC2	--	75	75	--	--	--
GC3	--	112.5	37.5	--	--	--
XC1	37.5	--	112.5	--	--	--
XC2	75	--	75	--	--	--
XC3	112.5	--	37.5	--	--	--
XL1	75	--	--	75	--	--
XA1	75	--	--	--	75	--
XD1	75	--	--	--	--	75
GL1	150	--	--	75	--	--
GA1	150	--	--	--	75	--
GD1	150	--	--	--	--	75
CL1	75	--	--	75	--	--
CA1	75	--	--	--	75	--
CD1	75	--	--	--	--	75

2.3 Fourier Transform Infrared Spectrometry:-[S.M. Al-Saidan et.al.]

Fourier transform infrared (FTIR) spectra of Ambroxol hydrochloride, Xanthan gum, Guar gum, κ-carrageenan gum, physical mixtures, were recorded on FTIR spectrometer (model FTIR-4100 Plus, Jasco).

2.4 Evaluation of Tablets:-[V. K. Guptaa et.al.]

The tablets were also evaluated as per IP1996 for weight variation (n=20), hardness (n=6), thickness (n=20), and friability. Hardness was determined by using a Monsanto tablet hardness tester (Campbell Electronics, Mumbai, India). Friability test was conducted using Roche friabilator (F. Hoffmann-La Roche Ltd, Basel, Switzerland). Thickness of the tablets was measured by digital Vernier calipers (Mitutoyo Corp, Kawasaki, Japan).

2.5 Determination of Drug Content:-[H. Santoset.et.al.]

Dissolve 0.300gms. of drug in 70ml. of alcohol and add 5ml. of 0.01M HCl.

Carry out Potentiometric titration using 0.1M NaOH. Read the volume added between two points of inflexion.

Factor –1ml.of 0.1M NaOH is equivalent to 41.46mg of Ambroxol Hydrochloride.

2.6 In Vitro Drug Release Studies:-[P.Colombo et.al.]
The release rate of ambroxol hydrochloride tablets was determined using USP Dissolution Testing Apparatus II (Paddle type). The dissolution test was performed using 900 ml of 6.8 buffer, at 37° ± 0.50°C and 100 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus hourly for 12 hrs, and the samples were replaced with fresh dissolution medium. The samples were filtered through Whatman filter paper no. 41. Absorbance of these solutions was measured at 248 nm. Cumulative percentage drug release was calculated using an equation obtained from a standard curve

2.7 Water Uptake Studies:-[D. S. Roy et.al., Nerurkar et.al., P. J. Cox et.al.]
Water uptake studies were performed by using equation stated by Roy and Rohera et al . The rate of test medium uptake by the polymer was determined by equilibrium weight gain method. The dry drug and polymer matrices were weighed, placed in dissolution baskets, and immersed in phosphate buffer (pH 6.8) maintained at 37±0.50 C in the dissolution vessels. At regular intervals, the pre-weighed basket–matrix system was withdrawn from the dissolution vessel, lightly blotted with a tissue paper to remove excess test liquid and re-weighed. The percent water uptake, i.e., degree of swelling, was estimated at each time point from using equation:

$$\text{Water Uptake (\%)} = \frac{Ws - Wi}{Wp}$$

Where,
Ws is the weight of the swollen matrix at time t, Wi is the initial weight of the matrix and Wp is the weight of the polymer.

2.8 Drug release kinetics[RW. Korsmeyer et.al.]
Data from the in vitro drug release were analyzed by different equations and kinetic models in order to evaluate the release mechanism of theophylline from the matrices. The software PCP Disso was used. The kinetic models used were
(a) Korsmeyer and Peppas model .

$$Mt / M\infty = k \times t^n$$

Where, Mt / M∞ is the fraction drug released, k is kinetic constant, t is the release time, n is the diffusional exponent for drug release.

Peppas claimed that, the above equation could adequately described the release of solutes from slabs, spheres, cylinders, and tablets (discs), regardless of release mechanism. Thevalue of 'n' gives an indication of release mechanism. When n = <0.5 the drug release follows fickian diffusion; and the value of n =>0.5<1.0 then anomalous non fickian release would be implicated. n is the slope value, of log Mt / M∞ vs log time curve.

b) Zero-Order Release :$Q_t = Q_0 + K_0 t$, where Q is the amount of drug dissolved in time t, Q is initial amount of drug in the solution (most times, $Q_0=0$) and K_o is the zero order release constant

c) First Order Kinetics : $\log Q_t = \log Q_0 + \frac{K_1 t}{2.303}$

d) Hixon-Crowell Model: $W_0^{1/3}$-$W_t^{1/3}$=Kst
e) Higuchi Model:$Q_t=K_Ht^{1/2}$

2.9 Stability Studies[B.R. Mathews et.al.]
Stability studies were conducted on Ambroxol Hydrochloride matrix tablets containing Xanthan gum, Guar gum and κ-Carrageenan gum to assess their stability with respect to their physical appearance, drug content, and drug release characteristics after storing in them Stability chamber (Thermolab) at 40°C/relative humidity (RH) 75% for 3 months

RESULTS

3.1Effect of gum type:-[S.M. Al-Saidan et.al., O. Sipahigil et.al., K.M. Picker et.al.]
The effect of Xanthan gum, Guar gum, κ- Carrageenan gum is shown in Figure No.01 .As the amount of xanthan gum in the matrix increased, there would be a greater degree of hydration with simultaneous swelling which results in a lengthening of the drug diffusion pathway and reduction in drug release rate. Among the different formulations X1 showed highest release of 76.85% in 12 h.

Guar gum has minimum water uptake and hence minimum swelling .At low concentrations of guar gum G1 a very rapid release of drug is observed. So more quantity of polymer concentration was required to achieve sustained release in case of Guar gum. In case of κ-Carrageenan gum,among the different formulations C1 showed release of 80.42% in 12 h. Due to its gelling property, it has been studied as a release retardant for ionic and nonionic drugs.Drug release decreases as swelling increases and Carrageenan gum swells rapidly and increases the drug diffusion pathway and hence causes reduction in drug release.

3.2 Effect of combination of Gums:-[S.M. Al-Saidan et.al., V. K. Guptaa, et.al.]
Combinations of Xanthan gum and Guar gum at different ratios are shown in Table No.01. As the amount of xanthan gum in the matrix increases a greater retardation of drug is observed. This may be due to the greater degree of swelling of Xanthan gum. As shown in Figure No.02 when the concentration of Guar gum in the matrix is increased a higher initial release as well as increased drug release for a period of 12h is observed. This is due to the low water uptake of guar gum as compared to xanthan gum. The formulation XG1 showed release of 92.67% in 12h.

When Xanthan gum and Carrageenan gum were combined at different ratios a greater retarding effect was observed at all the ratios. Xanthan and Carrageenan gum swell rapidly from the beginning of the dissolution and form a viscous gel as shown in Figure 02. Hence a prolongation of drug release is seen in all the combinations of Xanthan and Carrageenan gum. The formulations XC1, XC2 and XC3 showed 76.75%, 79% and 92.94% release for the period of 12h.
In the combination of Guar and Carrageenan gum shown in Figure No.02 it was seen that as the amount of Carrageenan gum in the matrix increases drug release is decreased. This may be due to the high initial water uptake and swelling of Carrageenan gum .Among the different combinations GC1 showed highest drug release of 95.71% in 12h.

Figure No.01:- Effect of concentration of gums on Ambroxol HCl release

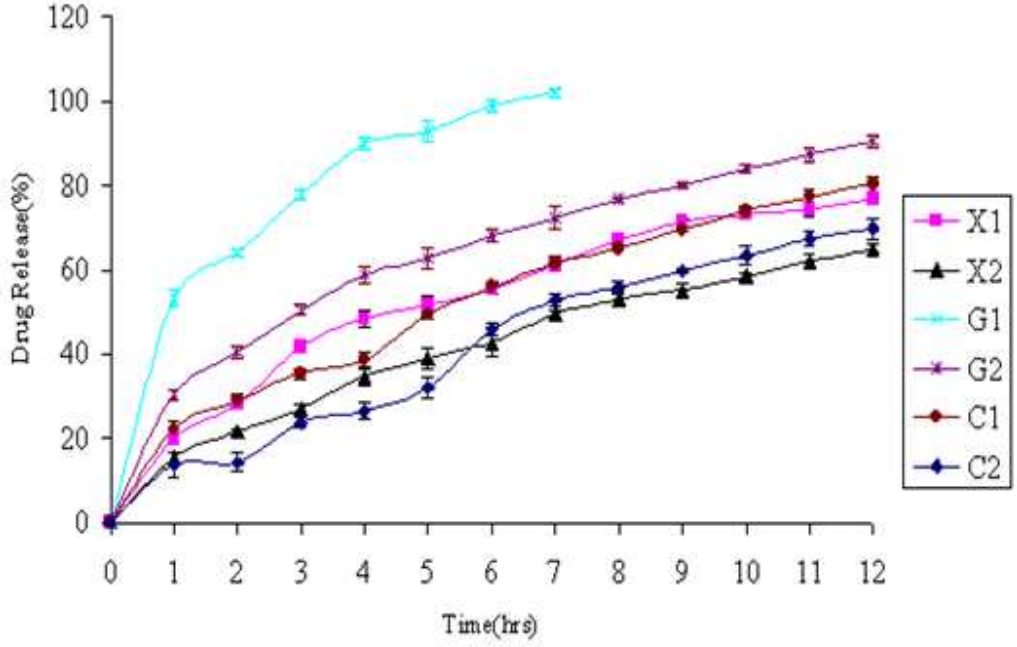


Figure No.02:- Effect of combination of gums on Ambroxol HCl release

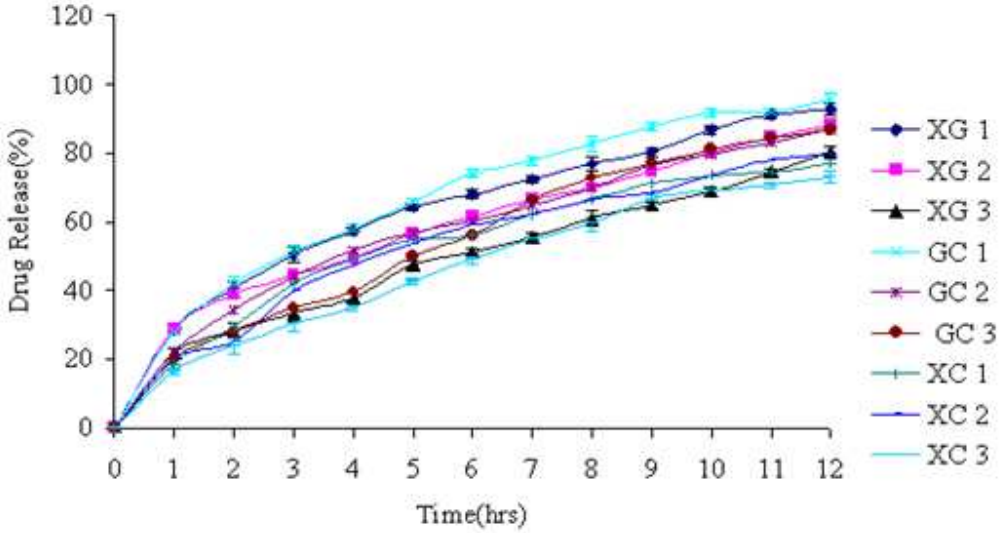
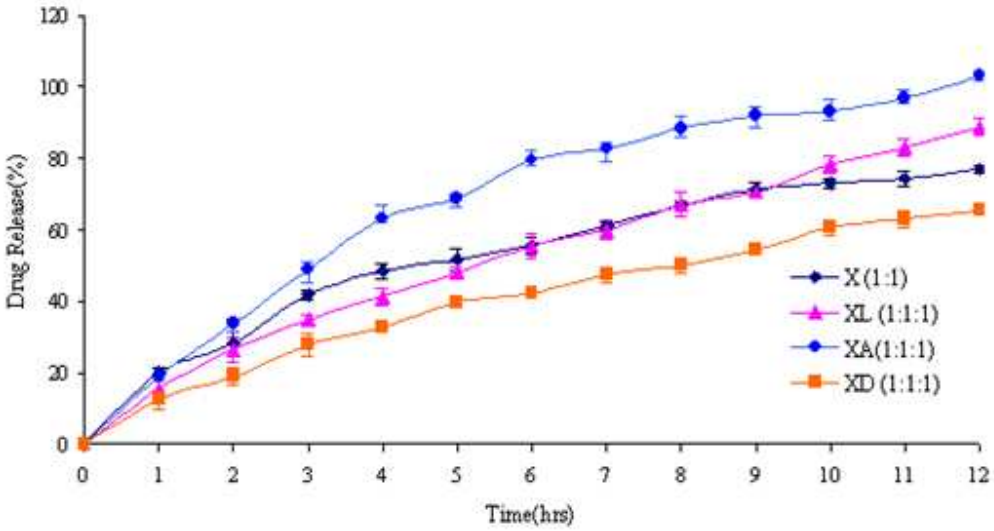


Table No. 02:- % Drug Release in 12 hrs, Diffusion Exponent (n) of Peppas Model and Regression Coefficient (r^2) of Ambroxol HCl Release Data From Studied Matrices According to Different Kinetic Models (n= 3)

Formulation Code	Zero Order	First Order	Matrix	Peppas	Hixon Crowell	n value	Best fit Model	%Release in 12hrs(%)
X1	0.8651	0.9834	0.9956	0.9921	0.9592	0.5504	Matrix	76.946±3.21
X2	0.9296	0.9895	0.9929	0.9975	0.9767	0.5979	Peppas	64.717±1.22
G1	0.7433	0.9564	0.9802	0.9920	0.9506	0.3534	Peppas	99.45 in 7hr
G2	0.7831	0.9903	0.9950	0.9986	0.9627	0.4399	First Order	90.414±3.14
C1	0.9184	0.9937	0.9960	0.9924	0.9860	0.5503	Matrix	80.266±1.11
C2	0.9783	0.9923	0.9555	0.9752	0.9926	0.7602	Peppas	69.767±3.13
XG1	0.8201	0.9865	0.9977	0.9988	0.9774	0.4658	Peppas	92.622±3.04
XG2	0.8466	0.9863	0.9981	0.9968	0.9739	0.4532	Peppas	88.207±3.45
XG3	0.9281	0.9888	0.9926	0.9924	0.9924	0.5423	Matrix	80.281±2.48
GC1	0.8320	0.9912	0.9973	0.9973	0.9873	0.4965	Matrix	95.592±3.15
GC2	0.8761	0.9931	0.9987	0.9973	0.9802	0.5343	Matrix	86.761±3.22
GC3	0.9525	0.9923	0.9834	0.9937	0.9962	0.6335	Hixon Crowell	86.793±2.77
XC1	0.8555	0.9805	0.9946	0.9891	0.9538	0.5624	Matrix	76.914±2.56
XC2	0.8897	0.9915	0.9942	0.9889	0.9731	0.5803	Matrix	79.408±1.87
XC3	0.9484	0.9958	0.9862	0.9969	0.9894	0.6339	Hixon Crowell	72.992±1.65
XL	0.9660	0.9770	0.9824	0.9993	0.9943	0.6894	Peppas	88.874±1.34
XA	0.8915	0.9123	0.9882	0.9838	0.9065	0.6627	Matrix	103.215±2.2
XD	0.9533	0.9954	0.9863	0.9978	0.9880	0.6743	Peppas	65.479±3.10
GL	0.7809	0.9909	0.9938	0.9948	0.9748	0.4235	Peppas	94.020±1.10
GA	0.8067	0.8699	0.9923	0.9883	0.9805	0.4708	Matrix	99.833±1.07
GD	0.8757	0.9821	0.9944	0.9836	0.9748	0.4528	Matrix	85.745±3.24
CL	0.9226	0.9855	0.9934	0.9930	0.9922	0.5717	Matrix	90.875±1.10
CA	0.9003	0.9435	0.9959	0.9931	0.8881	0.5241	Matrix	102.660±2.1
CD	0.9151	0.9798	0.9932	0.9945	0.9643	0.5872	Peppas	61.382±1.12

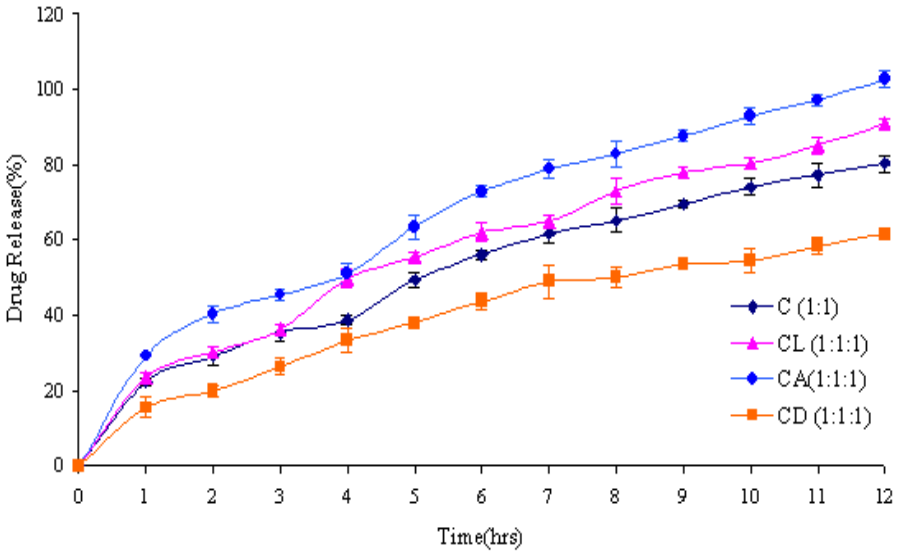
Figure No.03:- Effect of Diluent concentration on Xanthan gum matrices



3.3. Effect of Diluent on Release Characteristics:-

Water-soluble and water insoluble diluents at different concentrations can be successfully used to modulate the release rates from Xanthan gum, Guar gum and Carrageenan gum. The release profile of mini-matrices containing Avicel is higher than Encompress and lactose, respectively as shown in Figure 03. Maximum accumulated release of Ambroxol HCl at 12 h was 99.29%, for Avicel, 65.70%, for Encompress and 89.68% for lactose in Xanthan gum matrices.In case of Guar gum matrices it seems that the hydrophilic additives like Lactose mainly served to enhance water diffusion into the gel matrix and thus by implication diffusion of drug out of the matrix, resulting in rapid non-linear initial release of drug as shown in Figure 04. Drug release from Carrageenan matrices containing 1:1:1 ratio and different diluents (Lactose, Avicel 102 and dicalcium phosphate) .At the end of 12h, the percentage of drug release from Avicel 102 was 102.48% and DCP it was 67.70% at 1:1:1 ratio. As shown in Figure No.04.

Figure No.04:- Effect of Diluent concentration on κ Carrageenen gum matrices



3.4. Water Uptake Study:-[V. Velde et.al.]

Swelling index of matrices comprising of Xanthan gum, Guar gum, Carrageenan gum and combination of all the polymers is shown in Figures No.06 and 07.

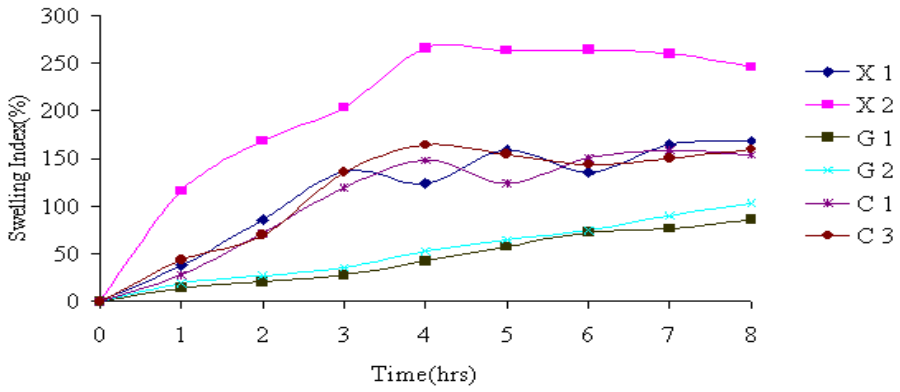
It is seen that as the amount of polymer in the matrix increases swelling increases for all the polymers. In the case of Xanthan gum maximum swelling is observed due to its excessive hydration ability with simultaneous swelling as shown in Figure No.06. In Xanthan gum high initial swelling is observed with erosion in the latter stages. Guar gum does not swell rapidly as it is in the case of Xanthan gum. Guar gum swells slowly initially and hence there initial burst release of drug from the guar gum matrices. Hence a more quantity of polymer is required to

achieve sustained release of drug from guar gum matrices as compared to Xanthan gum and Carrageenan gum matrices.

In case of Carrageenan matrices, high initial swelling is observed due to its its high hydration ability and forms a thick gel from which the drug diffuses .The swelling of Carrageenan matrices increases as the amount of polymer in the matrix is increased. In Carrageenan matrices high initial swelling is observed with erosion in the latter stage.

When Xanthan gum and Guar gum are combined together swelling increases as the amount of Xanthan gum in the matrices increases. The matrices containing more amount of Guar gum do not swell rapidly. When Xanthan gum and Carrageenan gum are combined together high swelling is observed due to excessive hydration of polymers. High swelling is observed in all the formulations containing Xanthan gum and Carrageenan gum. In case of Guar gum and Carrageenan gum, formulations containing excessive amount of Carrageenan gum swell excessively as compare to formulations having more amount of Guar gum.

Figures No.06:- Percentage Water uptake of Drug and plain polymer matrices:

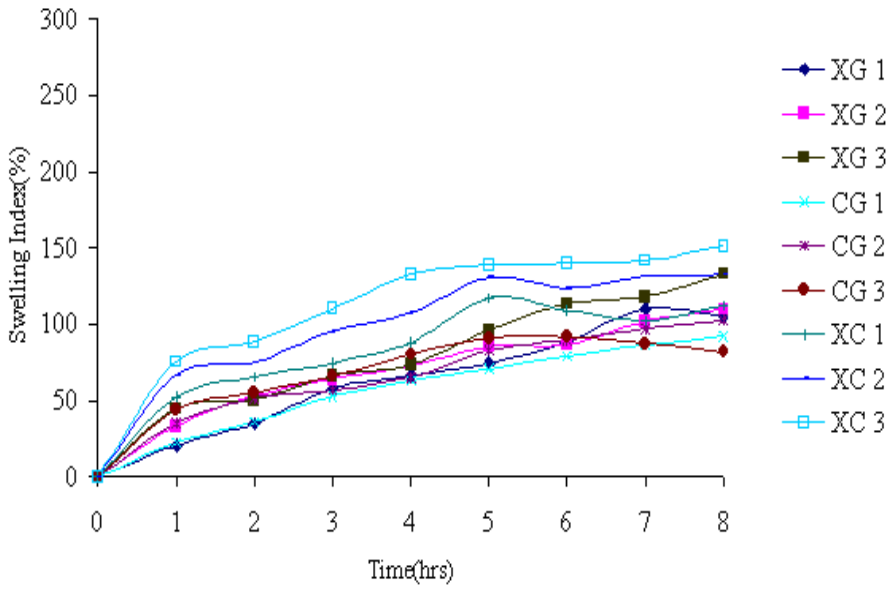


3.5 Stability Studies:-

At the end of the testing period, the matrix tablets were observed for changes in physical appearance, analyzed for drug content, and subjected to in vitro drug release studies.

No visible changes in the appearance of the matrix tablets were observed and a significant change was not seen in the drug content and drug release at the end of the storage period.

Figures No.-07:- Percentage Water uptake of Drug and combination of polymer matrices



DISCUSSION

The presence of anionic side chains on the xanthan gum molecules enhances hydration and makes xanthan gum soluble in cold water. At a fixed Ambroxol HCl dose, the total content of xanthan gum shows a dramatic change in their dissolution profile. When Xanthan gum is used as the only retarding polymer, drug release follows a Matrix type model and hence it can be concluded that the passage of drug is through the hydrated layer.To analyse the release mechanism of the drug through the matrix, Peppas equation was used .In case of Xanthan gum the n value was 0.5571 i.e.Anamalous transport or Non-Fickian diffusion which suggested that the drug release occurs by swelling as well as erosion. Three processes water penetration, gelatinization and diffusion for release of drugs from guar gum matrices are reported .As guar gum is a hydrophilic colloid it dissolves and forms pores filled with liquid from which drug can diffuse. In the case of Guar gum matrices, when Guar gum is used as the only retarding polymer, First order model is concluded. Guar gum dissolves and forms pores filled with liquid in which drug can thereafter diffuse .The drug release mechanism from Guar gum follows Fickian diffusion i.e. n value of 0.4423.This suggests that the drug release from the guar gum matrices is by water penetration, gelatinization and diffusion. Drug release decreases as swelling increases and Carrageenan gum swells rapidly and increases the drug diffusion pathway and hence causes reduction in drug release. In case of Carrageenan matrices, Matrix type model is concluded which shows that the passage of drug is through the hydrated layer .The drug release mechanism from the Carrageenan matrices showed Anamalous behaviour i.e.Non-Fickian diffusion with n value of 0.5633 which shows that the drug is released by swelling as well as erosion in the latter part of the dissolution period. **[**RW. Korsmeyer et.al.,T.Phaechamud et.al., F.Ughini et.al., M.

Fukuda et.al., L. Rosario et.al., S.M. Al-Saidan et.al., H. Idus et.al., V. K. Guptaa et.al.,M.Levina et.al.]

In case of combination of as the amount of xanthan gum in the matrix increases a greater retardation of drug is observed. This may be due to the greater degree of swelling of Xanthan gum. When the concentration of Guar gum in the matrix is increased a higher initial release as well as increased drug release for a period of 12h is observed. This is due to the low water uptake of guar gum as compared to xanthan gum .When Xanthan gum and Guar gum are combined together, the formulations with high concentrations of Xanthan gum XG 3 considering the erodibility of Xanthan gum, it may be concluded that the drug is released by erosion and diffusion within the matrix which is confirmed by the n value of 0.5420 which shows Non-Fickian diffusion. Decreasing the concentration of Xanthan gum XG 1 shifts the drug release kinetic to Higuchi model and shows Fickian diffusion.

When Xanthan gum and Carrageenan gum were combined at different ratios a greater retarding effect was observed at all the ratios. Xanthan and Carrageenan gum swell rapidly from the beginning of the dissolution and form a viscous gel. The viscosity of the gel layer plays an important part in controlling the release of the drug. Hence a prolongation of drug release is seen in all the combinations of Xanthan and Carrageenan gum. In case of Xanthan and Carrageenan gum matrices, a Non-Fickian release mechanism is observed for all the formulations. Hence, it can be concluded that the drug release from the Xanthan gum and Carrageenan gum matrices is by diffusion within the matrix as well as erosion.

In the combination of Guar and Carrageenan gum it was seen that as the amount of Carrageenan gum in the matrix increases drug release is decreased. This may be due to the high initial water uptake and swelling of Carrageenan gum .As the amount of Guar gum in the matrix increases drug release increased. In case of Guar gum and Carrageenan gum matrices, as the concentration of Carrageenan gum in the matrix is increased considering the erodability of Carrageenan gum the drug release mechanism follows Non-Fickian mechanism whereas at lower levels of Carrageenan gum a fickian diffusion is concluded.

The release mechanisms were anomalous (non- Fickian), with n values of 0.6894, 0.6627and 0.6743 for lactose, Encompress and Avicel respectively. There was little difference in release from the formulations containing Encompress and lactose Although Avicel and Encompress are water- insoluble excipients, their drug release profiles were different. The mini-matrices containing Avicel exhibited a higher drug release rate than those containing Encompress after the first 2 h. This could result from the disintegration property of Avicel. For mini-matrices containing Encompress, the contribution of Fickian diffusion predominated for the first 8.5 h of the dissolution period, and decreased gradually until polymer relaxation become predominant at the end.

Whereas with mini-matrices containing lactose, the contribution of Fickian diffusion predominated during the first 2 h, decreasing gradually until polymer relaxation became predominant. Lactose dissolution may create void spaces in the structure resulting in higher drug release rates (F. Lotfipour et.al.). On the other hand, with Avicel the contribution of polymer relaxation occurs almost exclusively throughout the entire dissolution time period. When in

contact with the dissolution medium, xanthan gum absorbs water, swells and becomes a hydrated gel. At the same time Avicel, having disintegration properties, promoted the disintegration of the mini matrices. The mini-matrices were therefore easier to erode, compared with Encompress, resulting in a higher release profile. In addition, studies have been performed showing that tablets produced with Encompress do not disintegrate readily so mini-matrices containing Encompress would have less tendency to erode, compared with Avicel, consequently showing a slower release profile.

In case of Guar gum matrices it seems that the hydrophilic additives like Lactose mainly served to enhance water diffusion into the gel matrix and thus by implication diffusion of drug out of the matrix, resulting in rapid non-linear initial release of drug. The presence of dicalcium phosphate in the matrix due limited solubility did not show a significant difference on the release profile of guar gum matrices. The mini-matrices containing Avicel exhibited a higher drug release rate than those containing Encompress and Lactose. This could result from the disintegration property of Avicel. The release mechanism was Fickian diffusion with n values of 0.4235, 0.4708 and 0.4528 for lactose, Encompress and Avicel respectively because of the minimal erodibility of the polymer even in presence of excipients.

In case of Carrageenan gum matrices, DCP retarded the release most due to its hydrophobic nature and as the quantity of DCP increased drug release was retarded .However water-soluble diluents like Lactose increased dissolution rate as the aqueous media penetrates into the matrix structure and dissolves the water-soluble diluent. The dissolved diluent moves off the matrix structure leaving void space and increasing tablet porosity. Avicel 102 due to its disintegrant action gives the highest release profile. The release mechanisms were anomalous (non- Fickian), with n values of 0.5717, 0.5241and 0.5872 for lactose, Encompress and Avicel respectively.

CONCLUSION

Xanthan gum and κ-Carrageenan gum have a greater ability to retard the drug release as compared to Guar gum due the greater swelling ability of Xanthan gum and κ-Carrageenan gum. The combination of natural gums with each other leads to greater release when Guar gum is used in greater concentrations and a greater retarding effect is observed with combinations of Xanthan gum and κ-Carrageenan gum. Hydrophilic diluents such as Lactose enhanced the drug release whereas hydrophobic diluents such as dicalcium phosphate retarded the release of the drugs and Avicel 102, being hydrophobic enhanced the dissolution of drug because of its disintegrating action.

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