WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 6.805
Volume 5, Issue 5, 1651-1666. Research Article ISSN 2277– 7105

DESIGN AND CHARACTERIZATION OF CONTROLLED RELEASE MICROCAPSULES OF ACARBOSE USING CELLULOSE POLYMERS

Dr. Abdul Hasan Sathali. A.* and Rajesh Kanna G.

Department of Pharmaceutics, College of Pharmacy, Madurai Medical College, Madurai- 625 020, Tamil Nadu, India.

Article Received on
16 March 2016,
Revised on 08 April 2016,
Accepted on 30 April 2016
DOI: 10.20959/wjpr20165-6226

***Corresponding Author**
Prof. Dr. Abdul Hasan Sathali A.
Department of Pharmaceutics, College of Pharmacy, Madurai Medical College, Madurai- 625 020, Tamil Nadu, India.

ABSTRACT

Controlled release microcapsules of acarbose were prepared by Coacervation phase separation technique using cellulose polymers (Ethyl cellulose, Hydroxy Propyl Methyl Cellulose k-15, Hydroxy Propyl Methyl Cellulose k-100 and Sodium Carboxy Methyl Cellulose). Microencapsulation of acarbose was done to achieve controlled drug release profile suitable for per oral administration. The Fourier Transform-Infra Red spectrum(FT-IR) and Differential Scanning Colorimetry(DSC) thermogram of pure drug and drug-polymer blend showed the stable character of Acarbose in the microcapsules. The prepared microcapsules were evaluated for different quality control parameter like; size analysis, drug content, encapsulation efficiency and drug release characteristics etc. Results of study revealed that Acarbose release from microcapsules greatly affected by different polymers with different core: coat ratio. A precise UV-Visible method also developed for the estimation of Acarbose in prepared dosage form. Microcapsules showing spherical surface, which was confirmed by scanning electron microscopy study. *In-vitro* dissolution studies indicated that drug release from microcapsules followed zero order kinetics; the release could be extended up to 12 hours, and non-fickian diffusion was involved.

KEYWORDS: Controlled release microcapsules, Acarbose, Cellulose polymers, Coacervation phase separation.

INTRODUCTION

Microencapsulation has been used in the pharmaceutical industry for the conversion of liquids to solids, taste masking of bitter drugs, acquiring prolonged or sustained release,

reducing gastric irritation and environmental protection of labile moieties.[1] Microcapsules having core material and coating material. Core material is the drug substance which is to be coated by a coating material generally polymers are used. An important class of polymer mediated drug delivery systems that are applied for controlled drug delivery is the microcapsules.[2,3] Microcapsules continue to be of much interest in controlled release based on relative ease of design and formulation and partly on the advantages of micro particulate system. Ethyl cellulose is a non biodegradable and biocompatible polymer most widely used as encapsulating materials for the controlled release of pharmaceuticals. Various techniques employed for Microcapsules Fabrication.[4]

Acarbose is O-4,6-dideoxy-4-{[(1S,4R,5S,6S) 4,5,6-trihydroxy-3-(hydroxymethyl)-2-cyclohexen1-yl]amino}-α-D-glucopyranosyl-(1→4)-O-α-Dglucopyranosyl-(1→4)-Dglucose, is an oral α-glycosidase inhibitor used in the management of non-insulin-dependent diabetes mellitus (NIDDM). It is obtained by fermentation processes from a microorganism, Actinoplanes utahensis. It delays the absorption of glucose in the small intestine by competing with the normal substrate for the binding site of the α-glycosidase enzyme and ceases the enzymatic reaction. This leads to a decrease in the formation and absorption of glucose in the blood stream. Acarbose has a short half-life ($t_{1/2}$ = 2 hrs), which necessitates repetitive administration of the drug i.e., 25 to 100 mg, 3 times a day. Thus, development of a modified release system of acarbose will obviate the need of multiple dosing of the drug candidate and hence improve patient compliance with reduced gastrointestinal side effects (flatulence, abdominal distension, borborygmus and diarrhoea) associated with repetitive administration of the drug.

Acarbose is an oligosaccharide with molecular weight of 645.6 daltons. The drug moiety lacks a chromophore and hence cannot be estimated directly by spectrophotometry and it was estimated by adding 1ml of 0.5 M NaOH then, 0.02 M $KMnO_4$ to the drug solution. After addition of 0.5 M NaOH and 0.02 M $KMnO_4$, the Polysaccharides on reaction with $KMnO_4$ in alkaline conditions yield manganate ions. Thus, reaction between the acarbose and alkaline $KMnO_4$ resulted in the formation of various oxidation products and green coloured manganate ions, which absorbs the UV-visible radiations.[5]

MATERIALS AND METHODS

Materials: Acarbose was obtained as a gift sample from Madras Pharmaceuticals Ltd. Ethyl cellulose, HPMC k-15, HPMC k-100 & Sod CMC was procured from Chemico laboratories (p) ltd, Mumbai, India. All other ingredients used were of an analytical grade.

Methods

Compatibility studies

Fourier Transform-Infra Red (FT-IR) Studies

The possibilities of drug–polymer interactions are investigated by FT-IR. The FT-IR graph of acrbose and combination of drug with polymer (Ethyl cellulose, HPMC K-15, HPMC K-100 and Sod CMC) are recorded. The analysis is performed by using (shimadzu FT-IR, Japan) spectrometer. The scanning range is 4000-400cm-1 and the resolution is 4cm-1sample is prepared in KBR pellets.[6]

Differential Scanning Colorimetric studies (DSC): DSC is performed using Q200 V24.4 thermal analyzer. The instrument is calibrated with indium standard. Accurately weighed (it varies from 3mg to 25mg) samples are placed in an open type ceramic sample pans. Thermo grams are obtained by heating the sample at a constant heating rate of 8˚C/minute. A dry purge of argon gas (60ml/min) is used for all runs. Samples are heated from 37˚C-9400˚C.[7]

Preparation of Controlled release microcapsules of Acarbose

Controlled release microcapsules of acarbose were prepared by Coacervation phase separation technique utilizing temperature change method. Briefly, individual cellulose polymer (Ethyl cellulose (insoluble in water, soluble in toluene), HPMCK15, HPMC K100 and Sod CMC) were dissolved in 25 ml of water which was previously heated at 50˚c, to this acarbose (250 mg) was added and stirred at 300 rpm with the help of magnetic stirrer for 15 minutes to get a stable dispersion. The dispersion was poured drop wise into the 50 ml of sunflower oil which was also previously heated to 50˚C on a water bath. The mixture was stirred with a help of magnetic stirrer at 300 rpm at room temperature for 2 hours. Finally it was kept in refrigerator for 24 hours to ensure the rigidness of microcapsules, then the microcapsules is washed with n-hexane. This Procedure was followed to prepare different core: coat ratios with different cellulose Polymers.[8,9] The compositions of the microcapsule formulations are listed in Table.1.

Table.1 Formulation of Controlled release acarbose microcapsules

S. No	Formulation code	Drug:Polymer Ratio	Drug	Ethyl Cellulose	HPMC K-15	HPMC K-100	Sod CMC
1	F1	1:1	250 mg	250 mg	-	-	-
2	F2	1:2	250 mg	500 mg	-	-	-
3	F3	1:3	250 mg	750 mg	-	-	-
4	F4	1:4	250 mg	1000 mg	-	-	-
5	F5	1:1	250 mg	-	250 mg	-	-
6	F6	1:2	250 mg	-	500 mg	-	-
7	F7	1:3	250 mg	-	750 mg	-	-
8	F8	1:4	250 mg	-	1000 mg	-	-
9	F9	1:1	250 mg	-	-	250 mg	-
10	F10	1:2	250 mg	-	-	500 mg	-
11	F11	1:3	250 mg	-	-	750 mg	-
12	F12	1:4	250 mg	-	-	1000 mg	-
13	F13	1:1	250 mg	-	-	-	250 mg
14	F14	1:2	250 mg	-	-	-	500 mg
15	F15	1:3	250 mg	-	-	-	750 mg
16	F16	1:4	250 mg	-	-	-	1000 mg

EVALUATION OF MICROCAPSULES

Percentage Yield

The percentage yield of the produced controlled release microcapsules is calculated for each batch by dividing the total weight of product (M) by the total expected weight of drug and polymer (Mo).[10]

$$\text{Percentage yield} = \frac{\text{Weight of microcapsules(M)}}{\text{Total expected weight of drug and polymer(MO)}}$$

Entrapment efficiency

100 mg of microcapsules were crushed in a glass mortar and pestle, and the powdered microcapsules of acarbose were suspended in water and then sonicated for 20 mins. It was shaken for another 20 mins for complete extraction of drug from the microcapsules. The mixture was filtered through 0.45 um membrane filter.[6] The suitable dilutions are made and estimated the content of acarbose spectrophotometrically at 611.40 nm. The drug entrapment efficiency was calculated using the following formula.

$$\text{Entrapment efficiency (\%)} = \frac{\text{Experimental drug content}}{\text{Theoritical drug content}} \text{ x } 100$$

Theoretical drug loading: Theoretical drug loading in Controlled release microcapsules is estimated by using the following formula,

$$\text{Theoretical drug loading (\%)} = \frac{\text{Weight of drug}}{\text{Weight of microcapsules}} \text{ x } 100$$

Experimental drug content: The weighed amount of drug loaded acarbose microcapsules were powdered and suspended in water and then sonicated for 20 mins. It was shaken for another 20 mins for complete extraction of drug from the microcapsules. The mixture was filtered through 0.45 um membrane filter.[11] The suitable dilutions are made and estimated the content of acarbose spectrophotometrically at 611.40 nm.

Determination of particle size distribution by sieve analysis

The particle size distribution of microcapsules was carried out using a mechanical sieve shaker. A series of five standard stainless steel sieves (Geologists Syndicate Pvt. Ltd, India) having mesh size of #18, #22, #40, #60 and #80 were arranged in an order of decreasing aperture size. Required amount of drug loaded microcapsules were placed on the upper most sieve. The sieves were shaken for a period of 10 min, and then the particles on each screen were weighed. The procedure was carried out three times for each product.[9,10] The parameters are shown in Table.2

Table. 2. Evaluation parameters of Controlled release acarbose microcapsules

S.No	Formulation Code	Percentage Yeild(%)	Particle Size In µm	Experimental Drug Content(%)	Theoritical Drug Loading(%)	Entrapment Efficiency(%)
1	F1	77.84	983.3	23.62	50	47.24
2	F2	80.14	965.4	20.06	33.3	60.24
3	F3	79.22	929.81	19.69	25	77.16
4	F4	80.34	931.19	14.54	20	72.7
5	F5	76.98	937.65	22.65	50	45.3
6	F6	77.24	986.96	17.62	33.3	52.91
7	F7	76.69	857.49	15.59	25	62.36
8	F8	79.13	836.01	12.73	20	63.65
9	F9	78	1003.05	34.97	50	69.94
10	F10	80.34	922.36	20.72	33.3	62.16
11	F11	81.02	1050.42	15.76	25	63.06
12	F12	81.24	991.74	9.52	20	47.62
13	F13	75.66	1065.73	29.48	50	58.08
14	F14	79.77	1045.56	17.42	33.3	52.38
15	F15	78.03	1036.26	15.23	25	60.92
16	F16	80.24	1020.31	13.42	20	67.1

***In-vitro* Release Studies**

In vitro release studies are performed in USP type I basket apparatus for 12 hours. The Microcapsules equivalent to 50 mg of acarbose were weighed and filled in the empty capsule shells and placed in the basket. The dissolution medium (900ml) consisted of 0.1M hydrochloric acid for first 2 hours and then changed to phosphate buffer pH 6.8 from 3rd to

12th hour. The basket is rotated at 75 rpm and temperature maintained at 37˚C. An aliquot 10ml was withdrawn at specific time intervals and replenished with an equivalent volume of dissolution fluid. Then, 1ml of 0.5 M NaOH and 1ml of 0.02 M $KMnO_4$ was added to the withdrawn samples.[5,12] Drug content was determined by UV-visible spectrophotometer at 611.40 nm. The release studies were conducted in triplicate shown in Table.3.

***In-vitro* kinetic release studies**

In order to investigate the drug release mechanism from Controlled release microcapsule formulations, the percentage cumulative drug release data is analyzed with following mathematical model,

1) Zero order-- $Q_t = Q_0 + K_0t$ (cumulative amount of drug released vs. time)
2) First order-- Log C = log C_0–kt / 2.303 (log cumulative percentage of drug remaining vs. time)
3) Higuchi Model-- $Q = kt^{1/2}$ (cumulative % drug remaining vs. square root of time)
4) Hixson Crowell-- $W_0^{1/3} – W_t^{1/3} = \kappa t$- (cube root of drug % remaining in matrix vs. time)
5) Korsmeyer- Peppas-- $M_t / M_\infty = K t^n$ (log cumulative percentage drug release Vs. log time) Where Mt / M∞ is a fraction of drug released at time t, k is the release rate constant and n is the release exponent. In this model, the value of n characterizes the release mechanism of drug.[13]

Release exponent (n)	Drug transport mechanism	Rate as a function of time
0.5	Fickian diffusion	t-0.5
0.45 < n-0.89	Non-fickian transport	t^{n-1}
0.89	Case II transport	Zero order release
Higher than 0.89	Super case II transport	t^{n-1}

Table. 3. *in-vitro* drug release profiles for prepared controlled release microcapsules of acarbose

Time in hrs	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15	F16
1	5.59	4.11	5.37	4.22	4.21	4.48	3.03	4.66	4.59	4.28	5.26	4.60	4.35	6.28	4.96	4.57
2	10.78	7.88	10.78	8.25	7.56	8.10	6.39	10.17	10.09	9.54	10.94	9.09	8.62	9.53	8.04	7.61
3	15.95	13.25	22.04	14.05	17.41	19.83	22.51	22.60	21.53	17.65	23.25	15.94	16.68	17.72	15.58	13.74
4	19.36	18.86	30.33	21.53	22.59	29.79	27.61	32.39	29.79	22.50	29.31	26.63	26.00	28.21	27.12	24.68
5	23.63	35.31	37.49	31.97	32.54	42.17	36.49	38.20	41.23	31.49	39.76	35.78	37.36	40.86	45.22	40.20
6	30.18	48.18	51.78	41.94	48.57	56.03	49.52	43.48	47.29	42.43	49.35	44.88	56.20	47.97	54.37	55.78
7	43.65	56.71	55.55	52.02	56.11	60.88	62.49	49.92	60.32	53.60	64.23	55.37	66.65	62.82	61.59	61.86
8	53.10	65.99	63.10	63.50	65.99	66.14	66.48	62.71	68.42	65.01	75.61	66.02	72.52	68.17	67.44	68.42
9	64.03	73.44	71.56	75.87	74.73	73.52	72.55	69.63	72.31	72.49	78.37	73.10	77.76	74.25	74.74	74.99
10	74.17	79.34	77.21	79.11	80.57	82.14	74.73	77.65	80.46	79.35	84.65	80.96	81.62	78.62	79.83	80.07
11	82.23	82.52	88.37	86.15	91.25	89.66	84.45	81.78	89.55	90.04	89.63	86.40	85.00	84.20	84.69	84.45
12	85.17	88.34	97.22	88.58	93.93	93.68	89.07	91.98	96.36	94.65	93.19	91.37	89.55	89.79	88.35	88.34

Swelling index

The swelling properties of the best formulation (F3) was determined in Phosphate buffer pH-6.8. An accurately weighed amount of microcapsules (50 mg) was placed in glass vial containing 10 ml of phosphate buffer pH 6.8 and allowed to swell at 37˚c, after 12 hours the swollen beads was removed and weighed. The wet weight of swollen beads was determined by blotting them with filter paper to remove moisture adhering on the surface, immediately followed by weighing on an electronic balance. The experiment was done in triplicate. The percentage of swelling was calculated from the following formula;

$SI\ (\%) = (Wt - Wo\ /Wt) \times 100$

Where, Wo –Initial weight of the microcapsules before swelling and,

Wt –Final weight of microcapsules after swelling.[14]

Infra Red spectroscopy studies

Infrared spectrum analysis for best formulation is carried out to find out the interactions between the drug and polymers used as per the procedure mentioned on drug and polymers interaction studies.

Surface Morphology of controlled release acarbose microcapsules by Scanning Electron Microscopy (SEM) technique

Scanning electron microscopy is an excellent tool for physical observation of morphological features of particle both initially and degradation process. It is helpful to examine particle shape and surface characteristics such as surface area and bulk density. The formulations are poured in a circular aluminium stubs using double adhesive tape, and coated with gold in HUS – 5GB vacuum evaporator and observed in Hitachi S – 3000N SEM at an acceleration voltage of 10 KV and a magnification of 5000X.

RESULTS AND DISCUSSION

In the present research work Acarbose was prepared into microcapsules with Ethyl cellulose, HPMCk-15, HPMCk-100 and SCMC to made as a controlled release formulations using Coacervation phase separation method. The FT-IR spectral analysis of Acarbose alone showed that principal peaks were observed at wave numbers 1629.85 cm-1, 1375.25 cm-1, 1155.36 cm-1, 3327.21 cm-1, confirming the purity of the drug.[15] In the FT-IR spectra of Drug Acarbose(Fig 1) and physical mixture of Acarbose and ethyl cellulose(Fig 2), Acarbose and HPMC K-15(Fig 3), Acarbose and HPMC K-100(Fig 4), Acarbose and Sod CMC(Fig 5), the major peaks of acarbose were observed at wave numbers 1629.85 cm-1, 1375.25 cm-1, 1155.36 cm-1, 3327.21 cm-1. It was confirmed that there are no major shifting as well as any loss of functional peaks between the spectra of drug and the physical mixture.

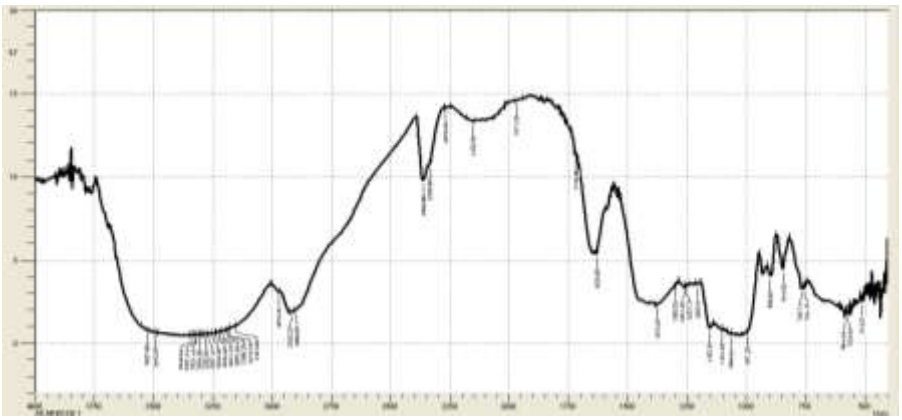


Fig. 1 FTIR Spectra of Pure drug

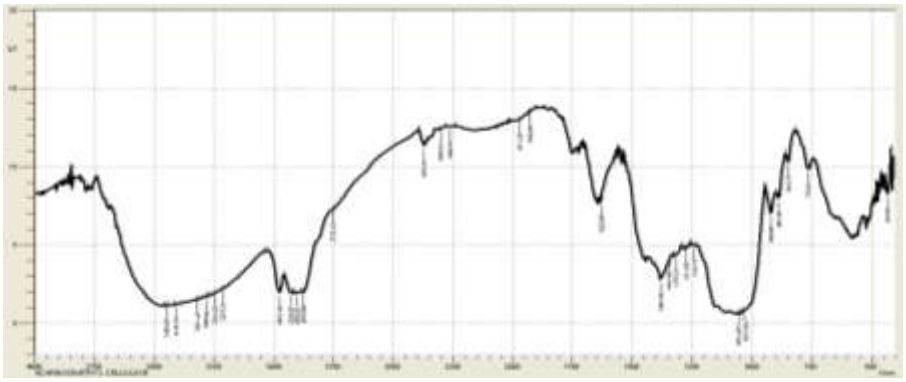


Fig. 2 FTIR Spectra of Mixture of Acarbose and Ethyl cellulose

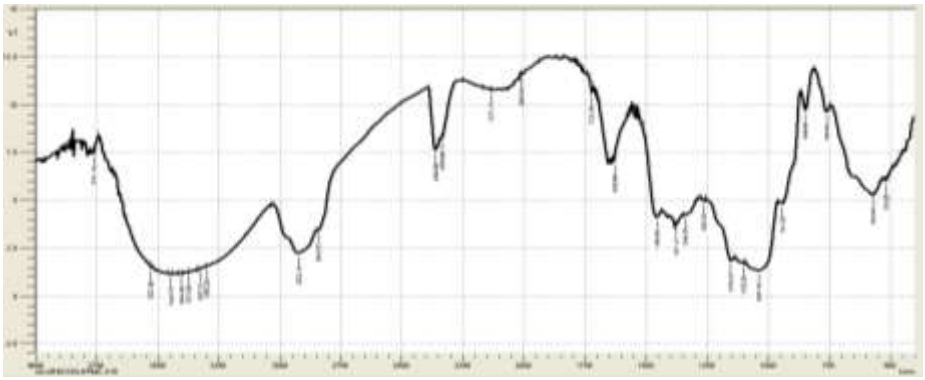


Fig. 3 FTIR Spectra of Mixture of Acarbose and HPMC k-15

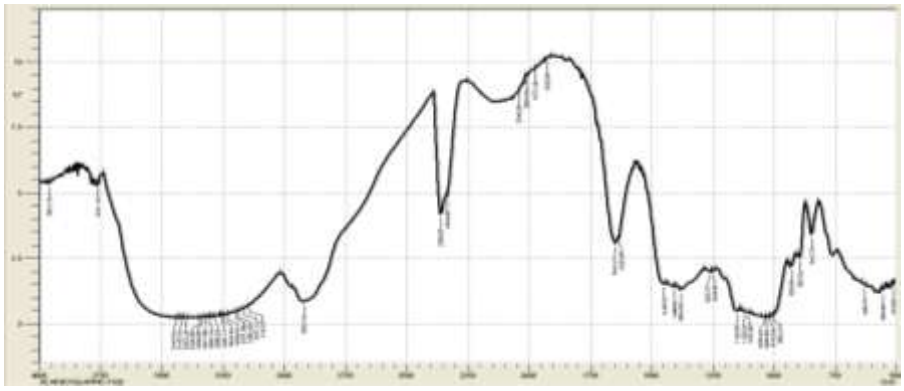


Fig. 4 FTIR Spectra of Mixture of Acarbose and HPMC k-100

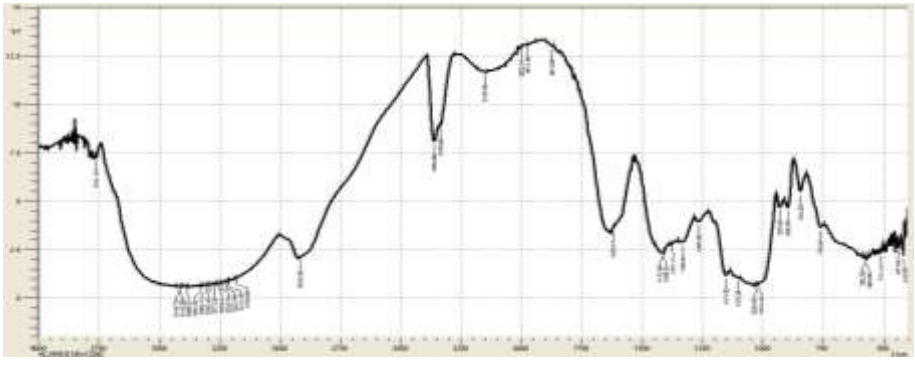
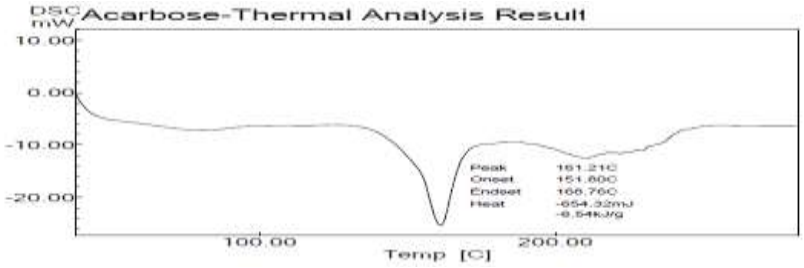
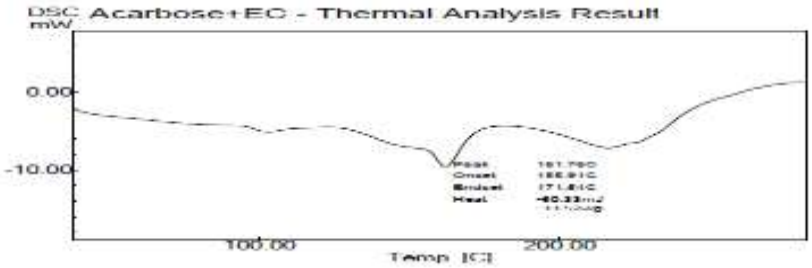


Fig. 5 FTIR Spectra of Mixture of Acarbose and Sod CMC

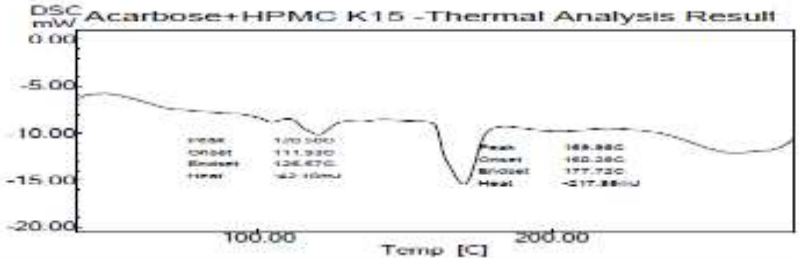
The DSC thermo grams of Acarbose alone showed endothermic tmax of 161.26°C, corresponding to the melting point of crystalline form of the drug Acarbose. The DSC thermo gram of Ethyl cellulose, HPMC and Sod CMC showed a sharp endothermic peak at 247.15, 104.57 and 102.53°C respectively, indicating the melting point of the polymer. An endothermic peak corresponding to the melting point of pure drug was important in all the drug polymer mixture, there was no change in the peak of acarbose, which suggested clearly that there was **no interaction** between the drug and the polymers and the drug was existed in its unchanged form.



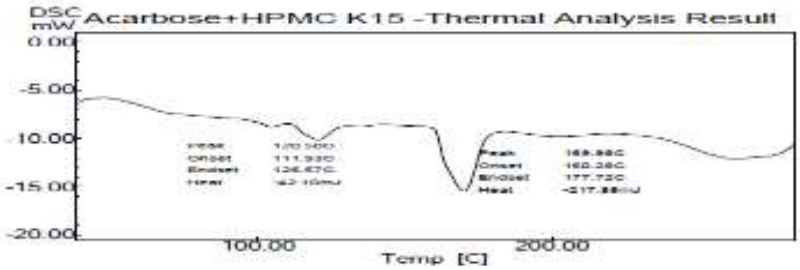
(A)



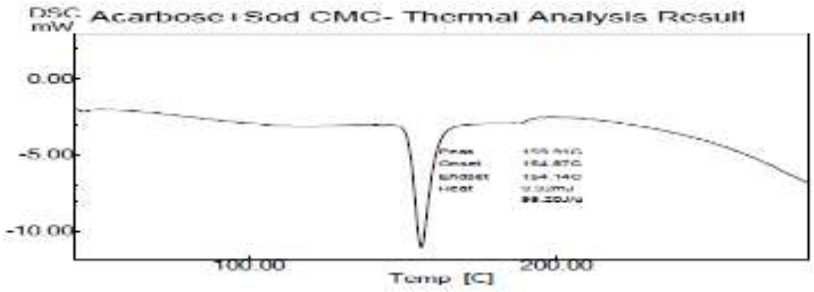
(B)



(C)



(D)



(E)

Fig. 6 DSC Thermo grams. (A) Pure drug, (B) Drug+ Ethyl cellulose, (C) Drug+ HPMC k-15, (D) Drug +HPMC k-100, (E) Drug+ Sod CMC.

The percentage practical yield of all the formulations (F1-F16) was found to be within the range of 77 to 81% which denotes the suitability of the method of formulation. Increasing polymer ratio in the formulation led to increase the product yield .The percentage practical yields of all the formulations are shown in Table.2. Prepared Microcapsules of Acarbose were evaluated for average particle size. The average particle size was found to be with the range of 836 to 1065 µm. So, the average particle sizes for all the formulations were within the range. The average particle size of all the formulations is shown in Table.2.

Prepared microcapsules were evaluated for entrapment efficiency. The entrapment efficiency was found to be with the range of 45 to 77%. Among the 16 formulations investigated formulation F3 (Ethyl cellulose 1:3 ratio), showed the maximum capacity for drug entrapment efficiency. The Entrapment Efficiency of all the formulations is shown in Table.2 The *in-vitro* release profile of Acarbose microcapsules prepared from different cellulose polymers are presented in Table.3. The cumulative percentage drug release after 12 hrs was found to be 85.17, 88.34, 97.22 and 88.58 for the formulations of F1 to F4, 93.93, 93.68, 89.07 and 91.98 for the formulations of F5 to F8, 96.36, 94.65, 93.19 and 91.37 for the formulations of F9 to F12, 89.55, 89.79, 88.35 and 88.34 for the formulation of F13 to F16. It was found that the drug release was prolonged up to 12 hrs.

The ethyl cellulose coated microcapsules exhibited good controlled release characteristics. The initial burst effect of some formulations may be due to presence of drug particle on the surface of the microcapsules, this initial drug release may also attribute as a desired effect to ensure Minimum effective concentration of drug to produce pharmacological action. The cumulative percentage drug release for formulations F1 to F16 as shown in Fig. 7.

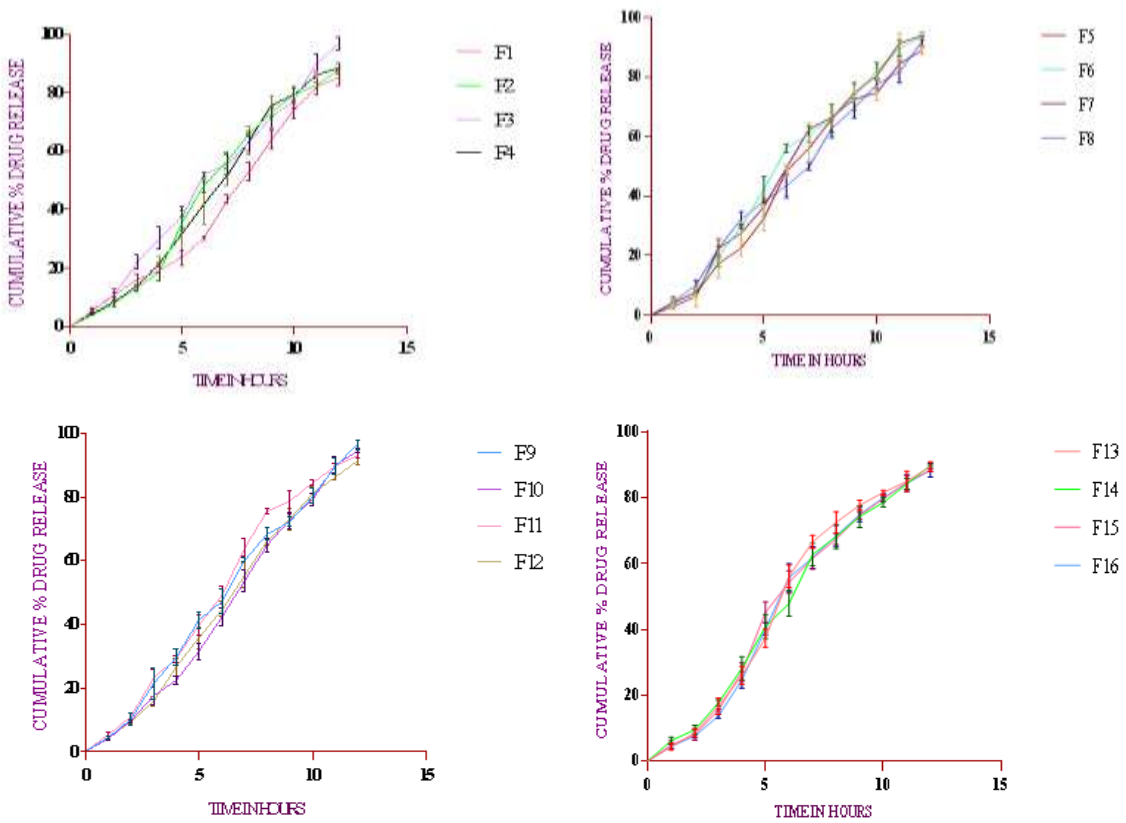


Fig.7 *In-vitro* Release Profile of Prepared microcapsules

The release data was modelled for Zero order, First order, Higuchi model, Hixson-Crowell model, Korsmeyer-Peppas model. The correlation coefficient of F1 to F16 formulations for Zero order, Higuchi, Hixson-Crowell and first order equations was shown in Table-4.

Formulation F3 (Ethyl cellulose 1:3 ratio) was found high correlation to zero order kinetics (0.997) as well as Higuchi plot (0.985) rather than Hixson-Crowell models. The release kinetics of all the formulations is best fitted the Higuchi model. Higuchi model with R2 values ranges from 0.914 to 0.985. From these higuchi model values, the release kinetics showed purely diffusion controlled. The drug release was proportional to square root of time, indicating that the drug release from polymeric (Ethyl cellulose) microcapsules was diffusion controlled. The data obtained was also put in Korsemeyer-peppas equation in order to find out release exponent (n value ranges is 0.410 to 0.691**),** which describes the drug release mechanism by Non Fickian diffusion.

From the above results of characterization F3 was selected as the best formulation, it was evaluated by swelling study. The formulation F3 was swelled in phosphate buffer p^H 6.8 for 12 hrs. Poor initial swelling in the first 4 hours, followed by relatively higher swelling till the

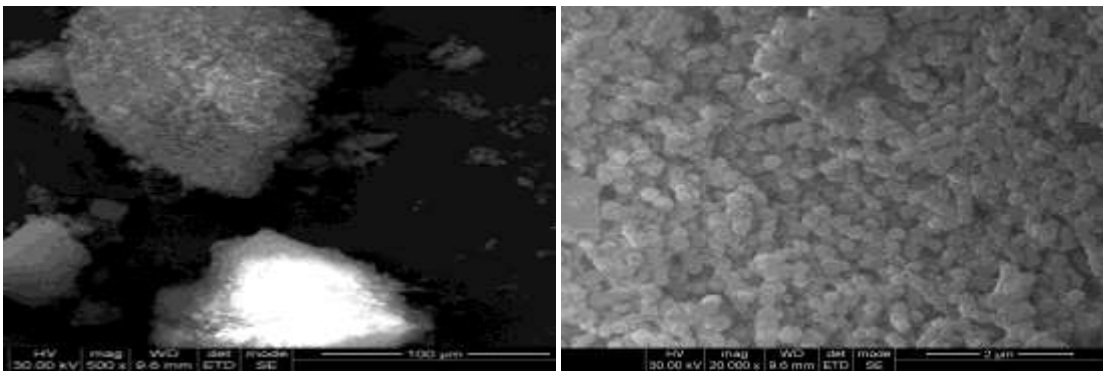
end of the period (12 hrs). Quantitative assessment of swelling for F3 formulation (Drug: Ethyl cellulose. 1:3 ratio) reported as percent swelling index was found to be 78.4%.

Table. 4 *In-vitro* kinetic data of Acarbose microcapsules

Formulation code	Zero order (R^2)	First order (R^2)	Higuchi model(R^2)	Koresmeyer-peppas(R^2)	Hixson-crowell(R^2)
FI	0.974	0.900	0.914	0.977	0.946
F2	0.977	0.964	0.962	0.980	0.985
F3	0.997	0.803	0.985	0.954	0.926
F4	0.985	0.943	0.957	0.971	0.976
F5	0.984	0.904	0.965	0.988	0.957
F6	0.990	0.928	0.983	0.939	0.982
F7	0.977	0.961	0.981	0.965	0.986
F8	0.994	0.900	0.978	0.986	0.955
F9	0.994	0.861	0.982	0.990	0.953
F10	0.993	0.878	0.958	0.957	0.954
F11	0.979	0.955	0.977	0.988	0.984
F12	0.992	0.939	0.972	0.977	0.987
F13	0.958	0.978	0.965	0.979	0.986
F14	0.979	0.966	0.976	0.980	0.990
F15	0.967	0.981	0.975	0.970	0.992
F16	0.964	0.979	0.968	0.971	0.991

The highest concentration (750 mg) of polymer showed highest swelling capacity because of that water uptake / binding ability is increases with increase in polymer concentration.

Scanning electron microscopy (SEM) exposed the distinct, spherical shaped microcapsules with rough surface and presence of holes /hollow cavity due to the collapse of the wall of the microcapsules during in situ drying process.[16] Thus the rate of solvent removal from the embryonic microcapsules exerts an influence on the morphology of the end product. Porous structure was observed on the surface due to the rapid diffusion of the solvent, there is a possibility of rupture of the capsule wall. SEM photographs were shown in Fig.8.



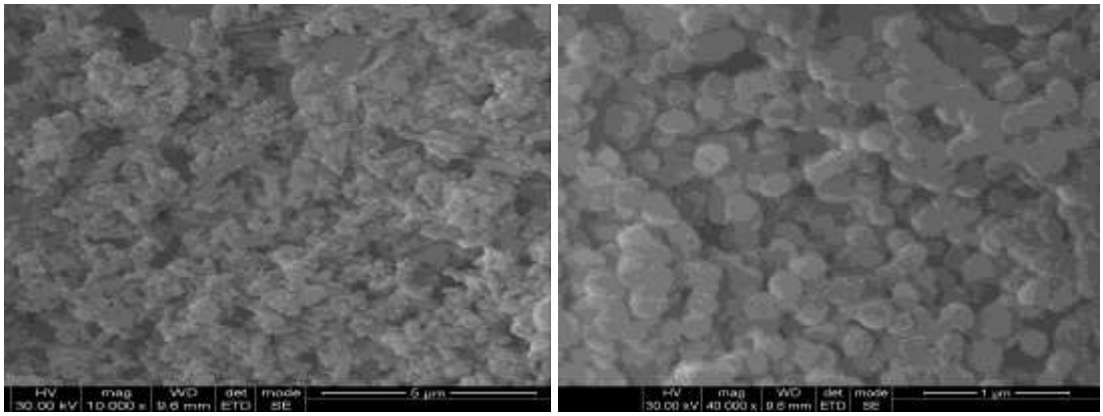


Fig. 8 SEM Photographs of Best Formulation

CONCLUSION

From this research it was concluded that the microencapsulation process can be considered as promising technique, which increase the duration of the drugs. From these studies it was concluded that acarbose loaded ethyl cellulose microcapsules prove to be a oral controlled delivery of acarbose for the management of non-insulin-dependent diabetes mellitus (NIDDM). Studies showed that, increase in polymer ratio increases the Entrapment efficiency of the drug candidate to the microcapsules. Since the drug was incorporated into ethyl cellulose coat showed controlled release of drug up to 12 hrs with good Entrapment efficiency. Thus the microcapsules as controlled release formulations can be useful for delivery of short elimination half life, low bioavailability and hygroscopic drugs through orally.

ACKNOWLEDGEMENTS

The authors are thankful to Madras pharmaceuticals, Chennai for providing the drug as gift sample. The authors are also thankful to Dr. P. Venkatesan, Annamalai university, Chidambaram and Dr. M. Rajan, Kamarajar university, Madurai.

REFERENCES

1. Niranjan Kumar Manna, Subas Chandra Dinda. Preparation and evaluation of mucoadhesive microcapsules of sodium valproate. IJPSR, 2011; 2(9): 2463-2468.
2. Suryakanta Swain, Aurobinda Behera, Sarwar Beg, Chinam N. Patra, Subash C. Dinda. Modified Alginate Beads for Mucoadhesive Drug Delivery System: An Updated Review of Patents. Recent Patents on Drug Delivery & Formulation, 2012; 6.

3. J.Sruti, C.NiranjanPatra, S.Swain, KCPanigrahi, APPatro, SBeg, SCDinda. Improvement in the dissolution rate and tableting properties of cefuroxime axetil by melt-granulated dispersion and surface adsorption. Acta Pharmaceutica Sinica, 2013; B 69-87.
4. Deepak K Mishra, Ashish K Jain, Prateek K Jain. A Review on Various Techniques of Microencapsulation. International Journal of Pharmaceutical And Chemical Sciences, 2013; 2(2): 962-977.
5. Vivek Ranjan Sinha, Ruchita V. Kumar. Utility of An Oxidation Reaction For The Spectrophotometric Determination of Acarbose In Controlled Release Tablets At Various Simulated Gastrointestinal Media. Acta Poloniae Pharmaceutica ñ Drug Research, 2012; 69(1): 23-32.
6. Meenakshi Joshi, Ruchi Tiwari, Gaurav Tiwari. Design And Development of Bilayer Tablet For Immediate And Extended Release of Acarbose And Metformin HCL. Drug Development and Therapeutics, 2015; 5(2): 93-108.
7. Rabel. S.R, Jona. J.A, Maurin. M.B. Applications of modulated Differential Scanning Calorimetry in preformulation studies. J. pharmaceutical and biomedical ananlysis, 1999; 339-345.
8. Anusha.N, Sanjay. K Mishra, Gopinath.S, Hindustan Abdul Ahad. Gastro Retentive Ranitidine Hydrochloride Microcapsules With Natural Polymers. International Journal of Institutional Pharmacy and Life Sciences, 2012; 2(1): 156-168.
9. Satyabrata Bhanja, Bibhuti Bhusan Panigrahi, Nilima Shukla, Danendra K Hardel, Muvvala Sudhakar. Formulation And InVitro Evaluation of Nicardipine Hydrochloride Microcapsules. Asian Journal of Pharmaceutical and Clinical Research, 2012; 5(3): 60-63.
10. Yadav.A.V, Shete.A.S, Dabke.A.P, Shinde.V.R. Formulation and In-vitro Evaluation of Aceclofenac Microcapsules. International Journal of PharmTech Research, 2009; 1(2): 135-138.
11. Prakash.K, Raju.P.N, Shanta.K.K, Lakshmi.M.N. Preparation and Characterization of Lamivudine Microcapsules Using Various Cellulose Polymers. Tropical Journal of Pharmaceutical Research, 2007; 6(4): 841-847.
12. Satyajit Panda, Snigdha Pattnaik, Laxmidhar Maharana, Girish Babu Botta, Prithwiraj Mohapatra. Formulation And Evaluation of Zidovudine Loaded Olibanum Resin Microcapsules: Exploring The Use of Natural Resins As Biodegradable Polymeric Materials For Controlled Release. Asian journal of pharmaceutical and clinical research, 2013; 6(3): 191-196.

13. Sivasankar Mohanty, G. Krishna Mohan, M. Sunitha Reddy. Formulation, Evaluation And Optimization of Sustained Release Microcapsules of Lornoxicam Prepared With Gum Dikamali & Pectin Extracted From Dillenia Indica. Int. J. Chem. Sci, 2015; 13(1): 97-106.
14. Sabitha.P, Vijaya ranta.J, Ravindra Reddy.K. Design and evaluation of controlled release chitosan-calcium alginate microcapsules of anti tubercular drugs for oral use. International Journal of Chemtech Research, 2010; 2(1): 88-98.
15. Clark. Clark's analysis of drugs and poisons. 3rd edition., 2: 568, 569.
16. Mominur Rahman.MD, Saiful Islam.MD, Nahid Sharmin, Jakir Ahmed Chowdhury, Reza-ul Jalil. Preparation and Evaluation of Cellulose Acetate Phthalate and Ethyl cellulose based Microcapsules of Diclofenac Sodium using Emulsification and SolventEvaporation Method. J. Pharm. Sci, 2010; 9(1): 39-46.