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DEVELOPMENT AND CHARACTERIZATION OF POLYMERIC MICROSPHERES FOR CONTROLLED DELIVERY OF GLIMEPIRIDE

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Abstract:

The purpose of the present investigation was to formulate and evaluate microencapsulated glimepiride produced by the solvent evaporation method, Method: Microspheres were prepared using Carbopol 934 polymers by solvent evaporation method an characterized for their micromeritic properties and drug loading, as well as by Fourier transform infrared spectroscopy (FTIR), Differential scanning calorimetry (DSC), X-ray Powder diffraction (XRPD) and scanning electron microscopy. In vitro release studies were performed in phosphate buffer (pH 7.4). Result: The resulting microspheres obtained by solvent evaporation method were white and free flowing in nature. The encapsulation efficiency was also found to be dependant on nature of polymer used in the formulation. The infrared spectra confirmed the stable character of glimepiride in the drug-loaded microspheres. Scanning electron microscopy revealed that the microspheres were spherical in nature. From the in vitro drug dissolution studies it was found that the sustaining effect of microspheres depended on the polymer concentration, amount of dispersant used and the type of polymer used in the formulation.

Key words: Microencapsulated, solvent evaporation method & by Fourier transform infrared spectroscopy.

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INTRODUCTION:

Microspheres have been widely accepted as a means to achieve oral1 and parenteral controlled release2 drug delivery system. The microsphere requires a polymeric substance as a carrier and a core material. Among the various methods developed for formulation of microspheres, the solvent evaporation method has gained much attention due to its ease of fabrication without compromising the activity of drug[1-3]. In the present investigation, Eudragit® RS 100 and Eudragit® RS 100 in combination with RL 100 microsphers were used as encapsulation materials. Eudragit ® RS 100 and Eudragit® RL 100 are referred to as ammoniomethacrylate copolymers, with the former having 5% functional quaternary ammonium groups and the latter having 10% functional quaternary ammonium groups. Eudragit® RS 100 is a water-insoluble polymer that is widely used as a wall material for sustained release microcapsules[4-8] . This is due to its biocompatibility, good stability, easy fabrication and low cost. The drug of choice, glimepiride, is an effective antidiabetic drug particularly in Type II diabetes (Non-insulin dependent diabetes mellitus). It is a secondgeneration sulfonylurea that actually lowers the blood glucose level in human by stimulating the pancreatic cell and thereby releasing the insulin. It has a short biological half-life of 3.4 ± 0.7 h2, 4 which make it more suitable to be designed as a controlled release formulation[9-12]. The main purpose of the present research was to develop a controlled drug delivery system of glimepiride for per-oral administration using biocompatible Eudragit® polymers in order to increase its biological half and to determine the influence of formulation and preparation variables on microparticle characteristics, such as drug incorporation and in vitro drug release rate.

MATERIALS AND METHODS:

Materials

GMP was received from Arandy Lab. Ltd (Hyderabad, India). Carbopol 934P (CP934P) was purchased from Loba Chemie Pvt. Limited, Mumbai. Acetone, n-hexane, Isooctane, span 80 and Span 85 were obtained from Merck Specialties Pvt. Ltd. (Mumbai, India). Other chemicals used were of analytical grade.

Methods

GMP-CP934P micro beads were prepared by Solvent Evaporation Technique (Liu et al., 2005). Different amount of CP934P was dissolved in 8.5 ml acetone separately by using a magnetic stirrer. GMP was added to the polymer matrix and mixed for 15 minutes. The resulting dispersion was added to a mixture of 90 ml light liquid paraffin (LLP) and contained 1% w/v span 80 in a 250 ml beaker, while stirring at 490 rpm using a mechanical stirrer. Stirring was continued for 45 minutes until the acetone evaporated completely. The micro beads formed were filtered using whatman no.1 filter paper. The residue was washed 4-5 times with 50 ml portions of n-hexane to wash the oil (LLP) completely[13-14].

Optimization is a process of making a formulation as perfect as possible within a given physical, chemical and biological cnsideration. The final product must meet the requirements from the standpoints of bioavailability, practical mass production and product reproducibility. Using a rational approach to the selection of a set of formulations, process variables are first selected and optimization is performed to quantify cntrolling variables of formulations. The steps involved in the optimization procedure are determination of the dependent variables, determination of the feasibility of using high and low levels of variables, performing statistically designed set of experiments, measurement of the response of interest, optimization by placing cnstraints on the model, graphical observation of plots and verification of the optimized formulation. There are several types of experimental designs that can be applied in the optimization of solid dispersion and micro beads formulation to test ingredients and/or to prepare or reformulate the product. Some of them are: full factorial design, fractional factorial design, central cmposite design, Face centered central cmposite design (FCCCD), Simplex lattice design and mixture design. Depending on the purpose, it is necessary to apply suitable design (Gonzalez, 1993). Response surface methodology (RSM) was initially developed and described by Box and Wilson (1951) (Hill and Hunter, 1966). Response surface methodologies are multivariate techniques that are mathematically fit in the experimental domain through a response function.

Drug Entrapment Efficiency (DEE)

Micro particles (25 mg) were pulverized and the powdered micro particles were suspended in 50 ml phosphate buffer (pH 7.4). After 24 h the solution was filtered and the filtrate was analysed by UV-VIS spectrometer (U-2001 Hitachi, Shiga, Japan) at 228 nm[15].

$$\text{DEE (\%)} = \frac{\text{Drug content as per assay x100}}{\text{Drug content as per initial load}}$$

Physical characterization

Micro beads/microspheres were characterized for their micromeritic properties such as particle size, shape, bulk density, tapped bulk density, cmpressibility index, Hausner's ratio, and angle of repose. The particle size of particles was determined with Leica-YM-750, Phase Cntrast

Dark Field laser light scattering instrument. Isobutanol was used as insoluble dispersion medium.

Bulk density / Tapped density is measured to determine _volume per unit mass‘ occupied by the micro particles at stationary state and under transportation state. It indicates free flow behavior of particles through the hopper. Angle of repose, Hausner‘s ratio, and Carr‘s index (% cmpressibility index) were determined to predict flowability. A higher Hausner‘s ratio indicates greater chesion between particles, while a high Carr‘s index (Palanisamy et al., 2009; Yadav et al., 2011) is indicative of the tendency to form bridges within hopper.

Solid state studies by instrumental analysis.

Fourier transforms infra-red spectroscpy (FT-IR)

FT-IR measurements were taken at ambient temperature using IR-Prestige-21 (Shimadzu, Kyoto, Japan) to investigate the possible chemical interactions between the drug and polymer matrix (Willard et al., 1992). About 2 mg of the samples were ground thoroughly with KBr and pellets were formed under a hydraulic pressure of 600 kg/cm. The scanning range was 4000-400cm-1.

Differential scanning calorimetry (DSC)

The DSC analysis was carried using Perkin Elmer Pyris Diamond TG/DTA analyser (Waltham, MA) to evaluate any possible drug-polymer interaction (Castelli et al., 2008). Standard operating procedure of this instrument was followed. Nitrogen gas was used as shield gas (at 40 psi). The DSC studies on the samples were performed by heating samples at a heating rate of 8oC/min over a temperature range of 30-3500C in closed aluminum pans under an argon purge[16].

Scanning Electron Microscpy (SEM)

Shape of particle was visualized by Scanning Electronic Microscpe. SEM was used to evaluate the shape and surface characteristics of particles (Gonzalez- Rodriguez et al., 2002). Scanning was done using a Jeol-make (UK) electron microscpe. Prior to examination the sample was fixed on a brass stub and cated with a gold palladium layer under argon atmosphere by using a gold sputter module in a high vacuum evaporator. The instrument was set at an excitation voltage 17 kv[17].

X-ray Powder diffraction (XRPD) studies

It is a physical technique used for the present study to identify on substances and other types of analysis principally for crystalline materials in the solid state (Castelli et al., 1994). It was done by using Rigaku Miniflex diffractometer (Rigaku C., Ltd., Tokyo, Japan) using a Kb filter, Cu radiation, at voltage of 30kV and a current of 15mA at 25°C. The sample was mounted on to the diffractometer and ciliated the X-rays on to the powdered sample to get the diffraction peak of certain intensities and recrded. Scan speed and scan axis were 1.000 deg/min and 2θ/θ respectively.

In vitro drug release profiles

The drug release study was carried out using (rotating basket, (Electolab, Mumbai,India) as per USP XXVI, 2003 (MaCusuCan et al., 2010) at 37 □ 0.50C at 100 rpm using 900 mL of phosphate buffer pH 7.4 as a dissolution medium (n=3). About 900 ml of dissolution medium was used which had been maintained at pH 1.2 for first 2 h, and phosphate buffer saline (pH 7.4) for the rest period of study(24 h for pectin beads, 18 h for CP934P beads and CP934P-ERL100 microspheres) and stirred at 50 rpm at 37°C. In each study, drug-loaded formulation cntaining 20 mg equivalent amount of GMP was used. Samples were withdrawn at intervals. sample (5 ml) was withdrawn carefully from the dissolution medium at various time intervals, and was replenished by an equal volume (5 ml) of fresh medium to maintain cnstant volume and sink cndition of dissolution medium. After filtering, each sample was analysed by spectrophotometric method (Hitachi, model U-2001) at a wavelength of 228 nm. The results measured in triplicate are expressed as percentage of the drug release.

RESULTS & DISCUSSION:

Effect of formulation variables on the measured responses

Cntrolling variables				% drug release	% DEE	% Yield
Batch Cde	drug- polymer ratio, (w/w)	surfactant cncentration ,(w/v)	stirring speed, rpm			
C1	1:1.5	0.70	460	64.23±1.09	61.50±1.19	66.69±0.76

C2	1:1.5	0.70	520	90.74±1.15	84.89±0.67	87.54±0.91
C3	1:1.5	0.90	490	77.08±0.45	73.34±1.94	79.42±1.34
C4	1:1.5	1.10	460	74.06±1.23	71.90±0.30	67.69±1.87
C5	1:1.5	1.10	520	98.83±1.56	92.31±1.19	98.01±0.92
C6	1:2.50	0.70	490	68.07±1.01	67.23±0.87	71.87±1.23
C7	1:2.50	0.90	460	64.65±0.57	60.88±0.99	64.76±0.93
C8	1:2.50	0.90	490	71.77±1.01	68.10±2.03	73.98±1.34
C9	1:2.50	0.90	520	95.77±0.88	87.16±1.32	93.50±1.50
C10	1:2.50	1.10	460	71.45±1.03	73.48±1.05	79.13±0.52
C11	1:3.25	0.70	460	61.23±1.25	59.84±0.86	62.54±0.49
C12	1:3.25	0.80	520	79.66±0.98	77.04±0.59	82.11±1.11
C13	1:3.25	0.90	490	65.64±0.45	64.23±1.29	68.60±0.49
C14	1:3.25	1.10	460	60.05±1.23	60.55±0.95	61.87±1.04
C15	1:3.25	1.10	520	83.48±0.84	81.13±1.30	82.66±0.65

Determination of yield (%) and DEE (%) of CP934P micro beads. Percent drug encapsulated was found to be in a range of 59.84-92.31% for CP934P micro beads and yield was varied from 62.54 to 98.01%. It was observed that low value of polymer concentration and high value of surfactant concentration and stirring speed produced high value of %DEE and % yield due to fast evaporation of acetone. %DEE was increased as the concentration span 80 was increased because dispersing agent decrease the interfacial tension between the lipophilic and hydrophilic phases of the emulsion and simplifies the formation of micro beads also this dispersing agent provides a thin protective layer around the droplets and reduces the extent of their collision and calescence. Loss of CP934P and drug in the dispersion medium was less in the form of fine particles and a maximum recovery (yield) of product (95.11%) was observed due to simple and rapid formation of micro beads.

Micromeritic characterizations of CP934P micro beads

The effect of particle size on bioavailability of drugs or their absorption in gastrointestinal tract is very important for pharmaceutical dosage form. Particle size characterization of formulation has becme one of the of the crucial aspects in drug product development and quality cntrol of solid oral dosage forms. The prepared micro beads are discrete with rough surface and more or less spherical in shape. Increase in the particle size (dp) was observed with the increase in drug-polymer concentration that might be due to more viscus nature of polymer solution which affected the performance spraying the mixture, causing formulation of large droplets. Decrease in the particle size was observed with increase in surfactant concentration (w/v). Generally the size of droplets in an emulsion is inversely related to the magnitude of shear stresses. Therefore, smaller micro beads are formed by increasing the stirring rate (rpm). The results obtained indicate that the effect of stirring speed is more significant than drug-polymer ratio which is evidenced in formulation C15. Particle size which was in the range of 714.56 to 832.30 µm was mainly governed by the drug-polymer concentration and stirring speed and slightly noticeable effect was noticed on particle size (dp) with surfactant concentration.

Table 5.3: Physical characterization of CP934P micro beads

Run number	Particle size(dp), µm	Bulk Density(BD), g/ml	Tapped Density(TD),g/m l	Angle of Repose (°)	Carr's Index(CI)	ausner Ratio
C1	836.29	0.744	0.821	28.44	9.59	1.15
C2	782.19	0.741	0.788	25.14	8.49	1.09
C3	796.80	0.724	0.780	25.67	9.72	1.16
C4	784.98	0.721	0.782	25.30	10.32	1.14
C5	724.19	0.716	0.811	25.45	11.96	1.14
C6	823.20	0.714	0.784	24.11	11.43	1.12
C7	833.09	0.642	0.712	25.70	10.19	1.17
C8	798.36	0.722	0.788	25.34	10.98	1.17
C9	822.27	0.655	0.733	25.70	10.90	1.19
C10	796.05	0.715	0.780	24.45	10.85	1.12
C11	752.01	0.721	0.782	24.30	10.32	1.14
C12	790.11	0.689	0.787	26.34	10.13	1.22
C13	842.56	0.689	0.796	25.05	11.16	1.20
C14	798.15	0.689	0.774	25.33	8.40	1.09
C15	754.66	0.744	0.820	25.23	9.48	1.01

Particle size which was in the range of 724.19 to 842.56 µm was mainly governed by the drug-polymer concentration and stirring speed and slightly noticeable effect was noticed on particle size (dp) with surfactant concentration. It was revealed that the BD, TD, angle of repose, Carr's Index (CI) and Hausner's ratio of formulations C1-C15 ranged from 0.642 to 0.744 g/ml, 0.713 to 0.821 g/ml, 24.11 º to 28.44º, 8.49 to 11.96 and 1.09 to 1.22 respectively.

***In vitro* study of drug release and release kinetics of CP934P micro beads**

The percentage of drug released from the micro beads was dependent on the physicochemical properties of the drug and controlling variables for the preparation of micro beads like drug-polymer concentration, surfactant concentration, stirring speed etc. Polymer concentration was important variables based on viscosity of the polymer solution. Study of *in vitro* drug release profiles are displayed in Figure 22. Study of drug release was performed for all 15 runs. *In vitro* drug release was performed in SGF (2h) and SIF (16h). It was observed from these profiles that drug release (C1-C15) was varied from 58.56 to 97.60% in 18 h. There are some reports on prolonged release of GMP from microspheres upto 24 h (Mahalaxmi et al., 2009; MaCusuCan et al., 2010; Gaba et al., 2011) in which method of preparation was quite time cnsuming and expensive in cmparison with that of present investigation.

Table 5.4: Cumulative % drug released from CP934P micro beads (C1-C5)

Time (h)	C1	C2	C03	C4	C5
0	0	0	0	0	0
1	4.03	4.12	4.45	4.71	5.98
2	6.03	7.61	6.21	7.98	8.11
4	8.23	12.36	10.16	12.79	13.81
6	12.13	20.93	18.04	21.46	22.99
8	18.66	31.24	29.07	32.84	35.03
10	29.35	47.19	41.05	46.95	52.45
12	43.49	63.40	53.01	59.79	70.32
14	55.04	77.10	63.68	67.91	83.10
16	60.02	85.24	70.21	70.78	92.17
18	62.24	88.75	75.09	72.07	97.60

Table 5.5: Cumulative % drug released from CP934P micro beads (C6- C10)

Time (h)	C06	C07	C08	C09	C010
0	0	0	0	0	0
1	4.27	3.24	4.24	5.32	4.62
2	6.41	5.23	7.23	8.68	7.94
4	8.81	7.73	12.03	13.14	12.32
6	12.57	11.73	20.44	21.23	21.28
8	19.21	17.68	31.35	33.98	32.54
10	30.12	28.88	45.68	49.89	46.55
12	44.17	42.50	57.57	66.31	59.25
14	55.23	52.68	63.32	80.99	67.17
16	62.22	57.22	67.05	90.99	70.23
18	65.86	59.66	69.78	93.31	71.25

Table 5.6: Cumulative % drug released from CP934P micro beads (C11- C15)

ime (h)	C11	C12	C13	C14	C15
0	0	0	0	0	0
1	3.20	4.57	4.44	3.12	4.14
2	5.02	6.88	6.68	5.05	6.30
4	7.43	10.78	8.90	7.51	10.57
6	11.44	18.28	12.94	11.35	19.52
8	17.45	29.88	19.06	17.34	30.02
10	28.35	41.89	29.91	28.36	43.15
12	42.22	53.21	43.97	42.23	58.32
14	52.22	64.02	56.88	52.08	71.18
16	57.03	71.30	61.77	56.32	78.39
18	59.24	77.03	63.65	58.56	81.23

The results showed that the rate of release of GMP from CP934P beads was mainly influenced by drug-polymer ratio (w/w) and stirring speed variables and slightly governed by surfactant concentration variable which was evidenced clearly in C5 (1:1.5,1.10,520) formulation. Span 80 was added as anionic surfactant to dispersion medium was found to be essential to minimize aggregation of micro beads.

The decrease in release rate with increasing content of the polymer can be explained by a decreased amount of drug present close to the surface and also by the fact that the amount of uncoated drug decreases with increase in polymer concentration. CP934P is cross-linked polyacrylate polymer (acrylic acid backbone). It easily opens up at lower concentration but at higher concentration it is less porous channel to exhibit the drug release. So diffusion from the swollen network is the rate controlling stage for the drug release from CP934P micro beads. Drug was released from pure GMP at faster rate than marketed SR tablet and formulation C5 (OPTZ).
Release study revealed that 99.68 % and 96.62% GMP was released within 8 h from pure GMP and marketed SR tablet whereas only 35.03 % drug was released in same period of time from optimized formulation (C5) and release of drug was extended over18 h. so, the prepared formulation is found to be more effective than available marketed product for the treatment of type-2 diabetes mellitus.

Table 5.7: Cumulative % drug released OPTZ micro beads, pure GMP and marketed SR tablet

ime (h)	C5(OPTZ)	Pure GMP	Marketed SR Tablet
0	0	0	0
1	5.98	50.68	28.06
2	8.11	73.89	48.12
4	13.81	90.52	67.31
6	22.99	99.51	84.85
8	35.03	99.68	96.62
10	52.45		99.78
12	70.32		99.92
14	83.10		
16	92.17		
18	97.60		

Solid state studies by instrumental analysis
Fourier transforms infra-red spectroscpy (FT-IR)

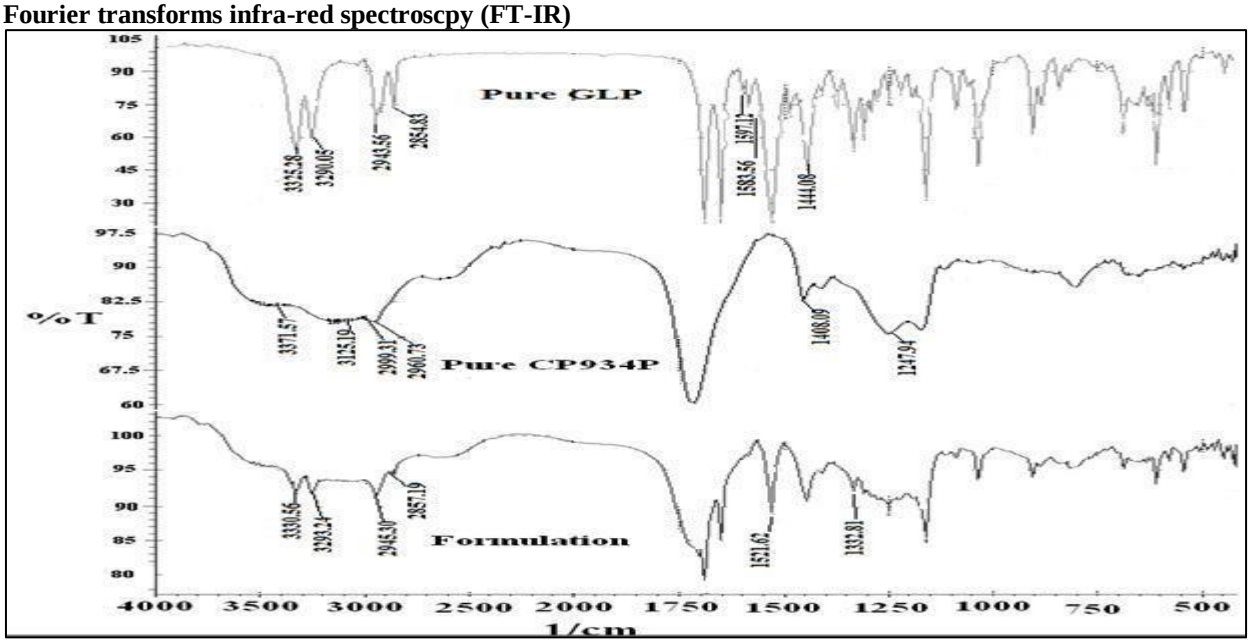
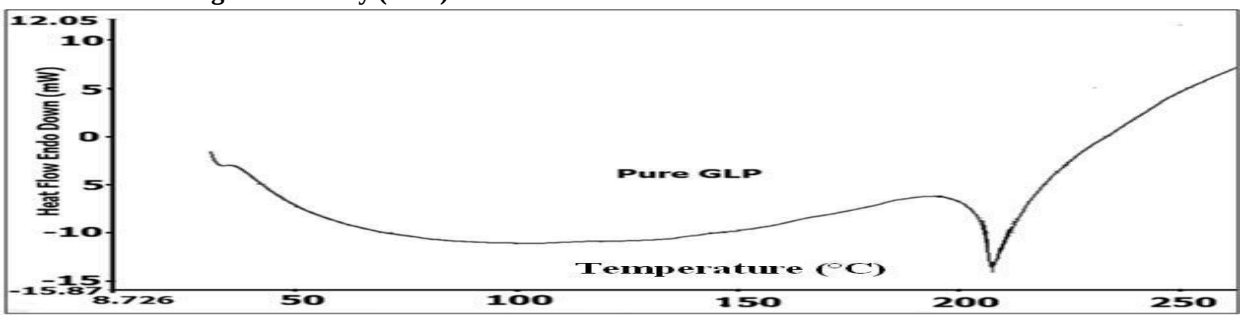
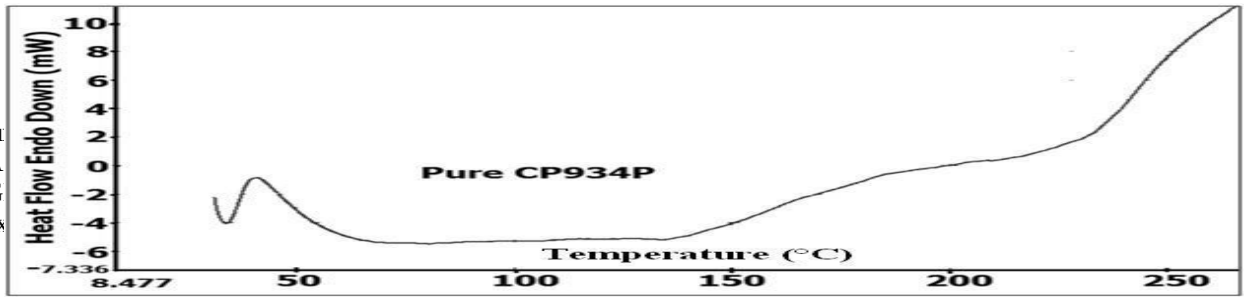


Figure 5.4: FTIR spectra of pure GMP, pure CP934P, and formulated micro beads (C5).
From the FTIR spectra it was confirmed that GMP and formulation components were compatible with each other**.**

Differential Scanning Calorimetry (DSC)





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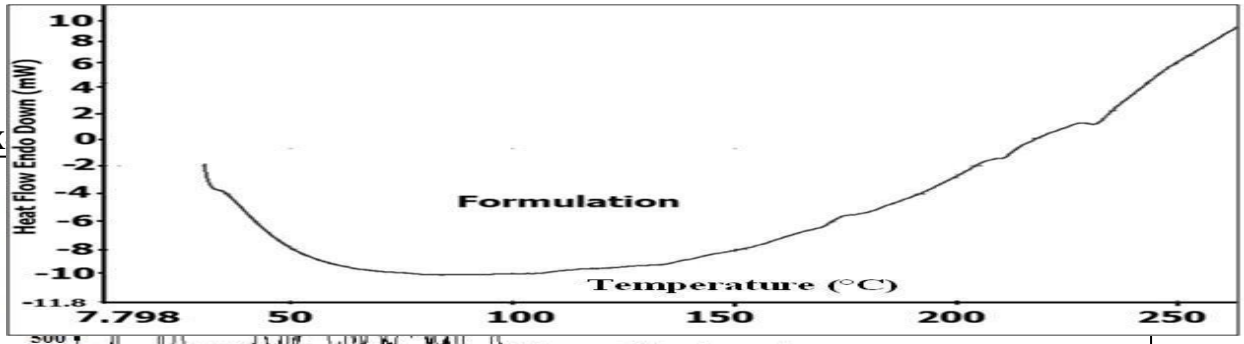

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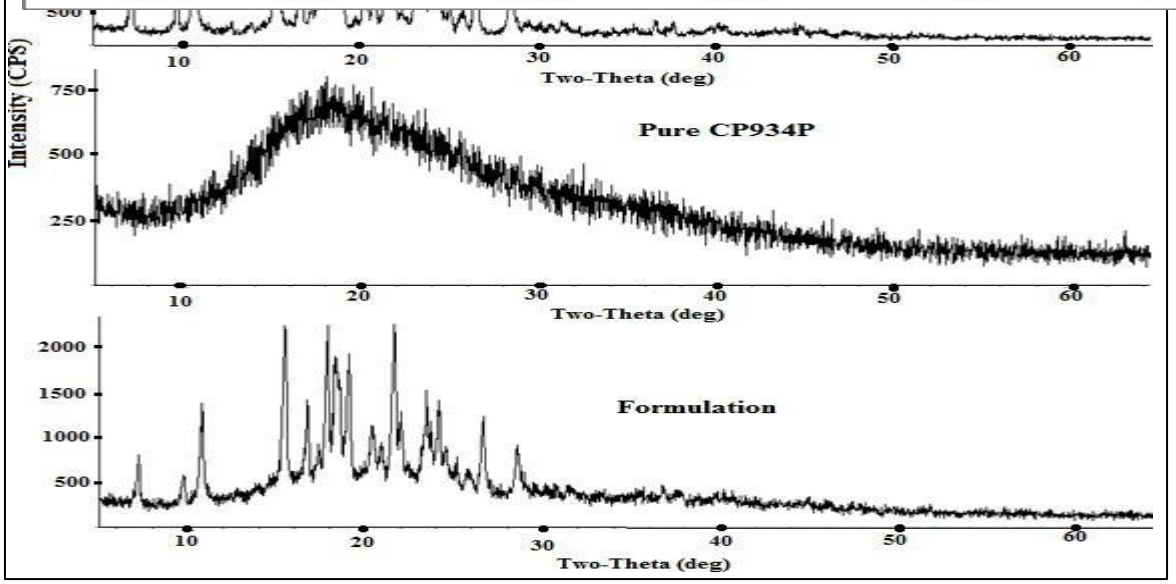

Figure 5.6: X-ray powder diffraCtion spectra of pure GMP, pure CP934P and formulated micro beads (C5).

This explicitly indicated that no interaction of the drug with the polymer occurred owing to encapsulation.

Surface characterization by SEM

Scanning electron microscpy represents the possible external morphology to appreciate both the quality and thickness of Coating materials. SEM revealed that the surface of selected micro beads is uneven and apparently dense.

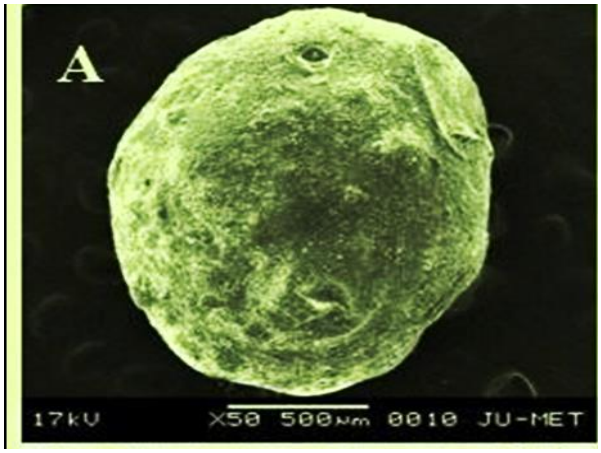

Figure 5.7: SEM micrographs of the micro beads (C5).

CONCLUSION:

Micro particles are established as unique carrier systems for many pharmaceuticals and can be tailored to acere to targeted tissue systems. Hence, microbeads and microspheresc can be used not only for controlled release but also for targeted delivery of drugs to a specific site in the body. Although significant advances have been made in the field of microencapsulation, there are still many challenges ahead in this field of particular importance are the development of cheaper biopolymers for the microencapsulation technology and the development of universally acceptable evaluation methods especially for bioadhesive microspheres. Therefore, the development of safe and efficient particular systems will require, in the future, indepth investigations of both the biological and technological aspects of these systems. Several methods and techniques are potentially useful for the preparation of mucoadhesive microparticles in the broad field of microencapsulation. The preparation method determines the type and the size of micro particle and influence the ability of the interaction among the Components used in micro particle formulations. Micro particles Containing drugs are employed for various purposes including but not restricted to Controlled drug delivery, masking the taste and odor of drugs, protection of the drugs from degradation, and protection of the body from the toxic of the drugs. Polymeric carriers being essentially multi disciplinary are commonly utilized in micro particle fabrication and they can be of an erodible or a non erodible type.

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Conflict of Interest

The authors declare no conflict of interest, financial or otherwise.

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REFERENCES:

1. Aly AM, Ali AS. (2010). Preparation and evaluation of Glimepiride tablets containing both enhanced and sustained release dosage dispersions. Int. J.Pharm. SCi. Nano.TeCH., 2(4):714-725.
2. Aminabhavi TM, Agnihotri SA. (2005). Development of novel interpenetrating network gellan gum-poly(vinyl alcohol) hydrogel microspheres for the controlled release of carvidilol. Drug Dev. Ind. Pharm., 31:491-503.
3. Arefin P, Hasan I, Shfiqul MI, Reza MS. (2016). Formulation and in vitro evaluation of eudragit RL100 loaded fexofenadine HCl microspheres. Bangladesh Pharm. J., 19(1): 58-67.
4. Duchene D, Touchard F, Peppas NA.(1988). PharmaceutiCal and medical aspects of bioadhesive systems for drug administration. Drug Dev. Ind. Pharm., 14:283-318.
5. Durig T, Fassihi R. (2000). Evaluation of floating and sticking extended release delivery systems: an unconventional dissolution test. J. Control. Release., 67:37–44.
6. Ezpeleta I, Arangoa MA, IraCHe JM, Staimesse S, CHabenat C, Popineau Y, OreCCHioni AM. (1999). Preparation of ulex europaeus lecitin-gelatin nanopatiCle conjugates and their Interactions with gastrointestinal muCus. Int.
7. J. Pharm., 191: 25-32.
8. Hill WJ, Hunter WG. (1966). A Review of Response Surface Methodology: A literature survey. Technometrics, 8(4): 571-590.

9. Hosmani AH, Kasture PV. (2009). Study of formulation variables on properties of Glimepiride mucoadhesive microspheres by faCtorial design. Lat. Am. J. Pharm., 28 (2): 254-60.
10. Ikeda K, Murata K, Kobayashi M, Noda K. (1992). Enhancement of bioavailability of dopamine via nasal route in beagle dogs. CHem. Pharm. Bull., 40(8):2155-2158.
11. Ginski MJ, Polli JE. (1999). PrediCtion of dissolution–absorption relationships from dissolution: CaCo-2 system. Int. J. Pharm., 177:117–125.
12. Gohel MC and Amin AF. (1998). Formulation optimization of Cntrolled release diclofenac sodium microsphere using factorial design. J. Control. release., 51: 115-122.
13. Gonzalez AG. (1993). Optimization of pharmaceutical formulations based on response surface experimental designs. Int. J. Pharm., 97: 149-159.
14. Gonzalez-Rodriguez ML, Holgado MA, Sanchez L, RabasCo AM, Fini A. (2002). Alginate/chitosan particulate systems for sodium diclofenac release. Int. J. Pharm., 232:225-234.
15. Jelvehgari M, Montazam SH. (2012). Comparison of microencapsulation by emulsion-solvent extraction/evaportion technique using derivative Cellulose and acrylate-methacrylate copolymer as carriers. Jundishapur J. Nat. Pharm. Prod., 7(4):144-152.
16. Jelvehgari M, Milani PZ, Khonsari F. (2014). Comparative study of in vitro release and mucoacesivity of gastric-compacts Composed of multiple unit system/bilayered discs using direct Compression of metformin hydrochloride. BioImpaCts., 4(1):29–38.
17. Jimenez-Castellanos MR, Zia H, Rhodes CT. (1994). Design and testing in vitro of a bioadhesive and floating drug delivery system for oral application. Int. J. Pharm., 105:65-70.