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Research Article

Effect Formulation Variables on Physicochemical Characteristics and Drug Release Potential of Oral Glipizide Microspheres

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ABSTRACT

In the present research work, guar gum (GG) microspheres containing glipizide were prepared by emulsification cross-linking method using polyvinyl alcohol (PVA) coating polymer and glutaraldehyde as a cross-linking agent. The physical state of the drug in the formulation was determined by Fourier transformation infra-red spectroscopy (FTIR) and differential scanning calorometry (DSC). The influences of process variables like concentration of polymer (s), copolymer, cross linking agent, surfactant, and plasticizer were evaluate on drug content, encapsulation efficiency, surface morphology, mean particle size, swelling ratio, mucoadhesive property and *in vitro* release studies. The shape and surface characteristics were determined by scanning electron microscopy (SEM). Particle size distribution was determined by standard sieve analysis. Particle size, shape and surface morphology, swelling ratio, drug entrapment efficiency and in-vitro release were significantly affected by concentration of guar gum, plasticizer and glutaraldehyde. FTIR and DSC studies revealed the absence of drug polymer interactions. The drug entrapment efficiency was obtained in the range of 81.30-94.24 %w/v. *In-vitro* drug release profile glipizide from microbeads was examined in simulated intestinal pH 7.4 at end of 12h. The mechanism of drug release from GG microspheres was diffusion controlled followed by First order kinetics and whereas GG-PVA coated microspheres approaching to near Zero- order kinetics.

Keywords: Glipizide, Guar gum, polyvinyl alcohol, emulsification, Glutaraldehyde, Zero-order kinetics

1. INTRODUCTION

Diabetes mellitus is a group of syndromes characterized by hyperglycemia; altered metabolism of lipids, carbohydrates, and proteins; and an increased risk of complications from vascular disease [1]. Orally active hypoglycemic drugs have an effectively lower blood glucose level which includes tolbutamide, glipizide, and metformin etc. Patients suffering from diabetes need to be on medication for long periods of time with constant plasma profiles to avoid the side effects [2]. Controlled release systems are gaining wide acceptance over conventional forms in the treatment of acute and chronic conditions like hypertension, diabetes etc. In addition to better patient compliance they have proved particularly valuable in ensuring continuous therapeutic effects. Techniques for incorporating drugs into polymeric microcapsules have gained considerable interest due to capability of achieving a controlled release [3]. Microencapsulation is a novel rapidly expanding technology to converting liquids to solids, by means of altering colloidal and surface properties, environmental protection and controlling the release characteristics or availability of coated materials [4]. The microspheres are characteristically free flowing powders incorporating a drug dispersed or dissolved throughout the polymer matrix have the potential for the controlled release of drug [5]. Glipizide is a second-generation sulfonylurea that can acutely lower the blood glucose level in humans by stimulating the release of insulin from the pancreas and is typically prescribed to treat type II diabetes (non-insulin dependent diabetes mellitus). Its short biological half-life (3.4 $\pm$ 0.7 hours) necessitates that it be administered in 2 or 3 doses of 2.5 to 10 mg per day [6]. Thus, glipizide is a very good candidate for the development of controlled-release dosage forms to avoid repeated administration and maintain constant drug release over prolonged period of time. Developments of several oral controlled drug delivery systems are based on several synthetic polymers to sustain the release of active material in different environment of GI-tract but they have certain disadvantages such as high cost, toxicity, poor biocompatibility, release of acidic degradation products, poor processing ability and rapid loss of mechanical properties during degradation and poor patient compliance [7]. Since natural polysaccharides comply with many advantages expected of pharmaceutical excipients such as non-toxicity, stability, more biocompatible, low cost, easy to degrade, swelling, availability and renewability they are extensively investigated for use in the development of solid oral controlled release dosage forms [8]. Guar gum is a naturally occurring non-ionic polysaccharide with long-chain, linear molecule of β-1,4-D-galactomannas with α-1,6-linked D-galactose has a molecular

weight of approximately 1 million, soluble in cold and hot water and it hydrates easily to produce gel dispersion with a greater low-shear viscosity than other hydrocolloids [9]. In pharmaceutical formulations, guar gum is used as binder and disintegrant, suspending agent, thickening agent and stabilizing agent. Guar gum is a potential hydrophilic matrix carrier for oral controlled drug delivery of drugs with varying solubility. Guar gum is compatible with most nonionic and anionic gums, featuring useful synergism with some synthetic polymers. It is soluble in salt solutions that contain up to 70% by weight of monovalent cation salts, stable between pH 4 to 11 and are susceptible to bacterial, heat, enzyme and UV degradation [10]. The aim of the present study was to develop sustained oral solid microspheres of glipizide using guar gum as carrier and PVA copolymer, glutaraldehyde as cross-linking agent and examine the effects of various process parameters on the physicochemical properties and drug release potential of the product

2. MATERIAL AND METHODS

2.1. Materials: Glipizide USP was obtained as a gift sample from Micro labs Bangalore**,** Karnataka, India. Guar gum LR and Glutaraldehyde solution 25% LR were purchased from Sd Fine Chem. Ltd. Mumbai, India. All other reagents and solvents used were of analytical grade satisfying pharmacopoeial specifications.

2.2. *Drug-Polymer Compatibility Studies*

2.2.1. Fourier transform- infrared spectroscopic analysis (FT-IR)

The compatibility between pure drug and polymer was detected by FT-IR spectra obtained on Perkin Elmer 1600 series, (USA). One to 2mg of glipizide alone, mixture of drug and polymer were weighed and mixed properly with potassium bromide uniformly. The spectra's were recorded over the wave number range of 4000 to 500 cm^{-1}.

2.2.2. Differential scanning colorimeter (DSC)

Thermograms were obtained by using a differential scanning colorimeter (Perkin Elmer) at a heating rate 10°C/min. over a temperature range of 30-250°C. The sample was thermatically sealed in an aluminum crucible. Nitrogen gas was purged at the rate of 100ml/min for maintaining inert atmospheres.

2.2.3. Preparation of Glipizide Microspheres

Microcapsules containing glipizide were prepared using GG and PVA alone and in combination as coat material(s). The required quantity of polymer (500 mg) was soaked in distilled water (20 ml) for 2 hrs and then mixed with sulphuric acid (0.5 ml of 1% v/v). The active substance glipizide (500 mg) and glycerin (30 % w/w of polymer) were dispersed uniformly with polymer solution. The aqueous polymer solution was emulsified by dropping (1 ml/ min) through a syringe with a needle number–18 (1.20x 38mm) into 200 ml liquid paraffin containing Tween-80 (0.5 % w/v) at 60^0C. Glutaraldehyde (2.5ml of 25 % w/v) concentrated with equal quantity of toluene was added as cross linking agent. Further the medium was stirred for 20 min at 500rpm and 60^0C. The formed spherical spheres were collected by decantation and washed twice with 20ml of n-hexane. The product was dried at room temperature for 12hrs and stored in desiccators [11]. Effect of certain processing variables like concentration of polymer, co-polymer, cross linking agent, surfactant on drug release potential were investigated for optimization of microspheres properties. The detailed composition of the various formulations mentioned in Table1.

2.3. Charecterization and Evaluation of Microbeads

2.3.1. Size analysis of microspheres

Different sizes in a batch are separated by sieving using a range of standard sieves 12/16, 16/20, 20/30 and the amounts retained on different sieves were weighed. Studies were carried out in triplicate [10]. The average size of the microspheres were calculated by using the equation

$$\mathbf{D}_{ave} = \sum \mathbf{X_i f_i} / \mathbf{f_i}$$

Xi = mean size of the range, *fi* = percent material retained on the smaller sieve in the size range.

2.3.2 SEM analysis

The particle size, shape and surface morphology of microspheres were examined by scanning electron microscopy. [Model LEICA S-430, London, U.K]. Microspheres were fixed on aluminium studs and coated with gold using a sputter coater SC 502, under vacuum [0.1 mm Hg]. Photographs were taken within a range of 50-5000 magnifications.

2.3.3. Estimation of Encapsulation Efficiency

Microspheres (100mg) were powdered; 50mg powder was dissolved in methanol in 50 ml volumetric flask and made up to volume. The solution was kept for 1hr with occasional shaking. Further 1ml of solution was diluted up to 100 ml with phosphate buffer pH 7.4. The content was analyzed spectrophotometrically at 276nm against blank [12]. The studies were carried out in triplicate. The encapsulation efficacy was calculated using the formula.

Drug Entrapment Efficiency = [Estimated drug content /Theoretical drug content] x 100

Table 1: Various formulations of glipizide microspheres

Batch code	D: P Ratio (% w/w)	Polymer: Co polymer (% w/w)	Drug + GG + PVA (mg)	Cross-linking agent (ml)	Tween-80 (% w/v)
M1	1:0.5	-	666.66+333.33+000	-	-
M2	1:1	-	500+500+000	-	-
M3	1:1.5	-	400+600+000	-	-
M4	1:1	1:1	500+250+250	-	-
M5	1:1	2:1	500+330+165	-	-
M6	1:1	3:1	500+375+125	-	-
M7	1:1	1:1	500+250+250	2.0	-
M8	1:1	1:1	500+250+250	2.5	-
M9	1:1	1:1	500+250+250	3.0	-
M10	1:1	1:1	500+250+250	2.0	0.1
M11	1:1	1:1	500+250+250	2.0	0.2
M12	1:1	1:1	500+250+250	2.0	0.4

Drug: Glipizide, GG: Guar gum, PVA: Polyvinyl alcohol

2.3.4. Swelling studies

A known weight (50mg) of microcapsules was placed in a glass vial containing 10 ml of phosphate buffer of pH 7.4 at 37± 0.5°C in incubator with occasional shaking. The microcapsules were periodically removed, blotted with filter paper and their changes in weights were measured during the swelling until equilibrium was attained. Finally, the weight of the swollen microcapsules was recorded after a period of 4hrs, and the swelling ratio (SR) was then calculated from the formula [13]. The studies were carried out in triplicate.

$$\text{Swelling Ratio (SR)} = \frac{We - Wo}{Wo}$$

Wo = initial weight of the dry microspheres, We = weight of the swollen microspheres at equilibrium swelling in the media.

2.3.5 In vitro wash-off test

The mucoadhesive property of microspheres was evaluated by an *In vitro* adhesion testing method known as wash-off method**.**

Freshly excised piece of intestinal mucosa (2 x 2 cm) from albino rat were mounted on to glass slides (3 x 1 inch) with cyano acrylate glue. Two glass slides were connected with a suitable support, about 25 microspheres were spread on to each wet rinsed tissue specimen and immediately thereafter the support was hung on to the arm of a USP tablet disintegrating test machine. When the disintegrating test machine was operated, the tissue specimen was given slow, regular up-and-down moment in the test fluid (900ml phosphate buffer of pH 7.4) at 37°C. At the end of 30 min, at the end of 1hr, and at the hourly intervals up to 4 hrs, the machine was stopped and number of microcapsules still adhering to tissue was calculated [14]. The studies were carried out in triplicate.

2.3.6 In vitro dissolution studies

The release of glipizide from microspheres was investigated in phosphate buffer of pH 7.4 as a dissolution medium (900 ml) using the rotating basket method specified in USP XXIV (Model-TDT6P-Electrolab). The drug loaded microspheres (equivalent to 10mg glipizide) filled in empty capsule shells were put into the basket rotated at a constant speed at 50rpm and maintained temperature 37^0C was maintained throughout the experiment. At fixed intervals, aliquots (5 ml) was withdrawn and replaced with fresh dissolution media. The concentration of drug released at different time intervals was then determined by measuring the absorbance using Hitachi U-2000 spectrophotometer at 276 nm against blank [15]. The studies were carried out in triplicate. The basic *in vitro* release data of selected microspheres was graphed as: Cumulative percent drug released vs. time.

2.3.7. Kinetics of drug release

In order to understand the mechanism and kinetics of drug release, the drug release data of the *in-vitro* dissolution study was analyzed with various kinetic equations like zero-order (% release v/s time), first- order (Log % retained v/s time) and korsmeyer and peppas equation. Coefficient of correlation (r) values were calculated for the linear curves obtained by regression analysis of the above plots [16].

3. RESULTS AND DISCUSSION

3.1. FT-IR studies

The compatibility between drug and polymer was confirmed by using FTIR spectroscopy. Figure 1(a) shows the IR spectra of pure drug glipizide with its peak as KBr (cm^{-1}), 3326 and 3251 (NH-CO-NH and CONH stretching); 3030 (aromatic C-H stretching); 2855, 2915 (C-H stretching of CH_2 groups); 1689 (CO_7 NH-CO-NH); 1650 (CO_7 CONH); 1598 (C=N

stretching); 1583, 1527, 1484 (C=C aromatic ring stretching); 1409 (C-N stretching) and 840 (1,4 disubstitued phenyl ring). Figure 1(b) shows IR spectra of formulation GG-PVA microcapsules (M4) containing glipizide. The IR (KBr) cm^{-1} spectrum of the formulation (M4) is not clearly split because of poor resolution of the groups. One of the reasons may be that the formulation under investigation might have absorbed moisture from the atmosphere and prevent the proper resolution of the bands for different groups [17]. However we can assume that NH groups of CONH and NH-CO-NH of the drug must have merged with broad peak appearing almost in the same range 3250-3400. The remaining absorption peaks for aromatic C-H stretching, C=O stretching, C=C ring stretching though did not appear exactly at the same frequency, however they are almost in the same expected range. Hence there is no change in the characteristic properties of the drug and its formulation indicates no interaction between drug and polymer.

3.2. Differential Scanning Colorimetry (DSC)

Figure 1(c) shows the DSC thermogram of pure drug glipizide with onset at 211.61°C and maximum occurring at 214.95°C. Figure 1(d) shows the DSC thermogram of formulation GG-PVA microcapsules (M4) containing glipizide with onset at 205.55°C and maximum occurring at 221.44°C. DSC study revealed that the thermograms of the pure drug and its formulation are almost identical. This indicates that there are no changes in thermal behavior of drug and the formulation samples.

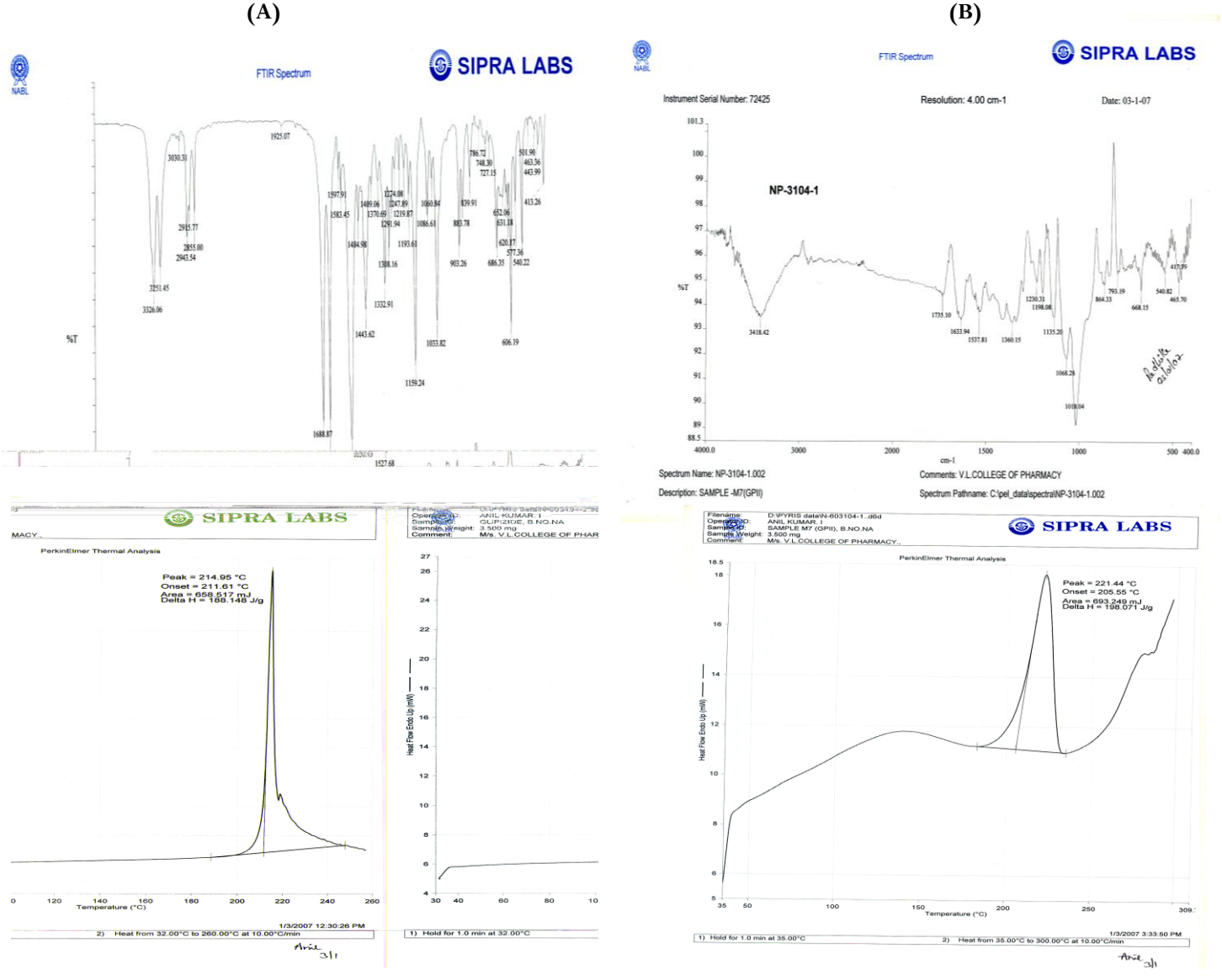


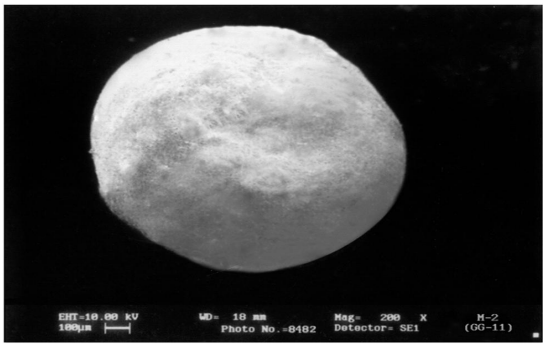
Figure 1.IR-spectra (a) Glipizide pure drug (b) GG-PVA drug loaded microspheres (M4) (c) DSC thermo-grams Glipizide pure drug (d) GG-PVA drug-loaded microspheres (M4)

3.3. Size analysis

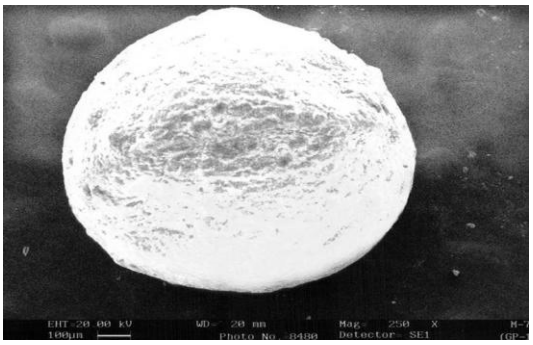
Particle size is inversely proportional to surface area and thus affects drug release from microspheres. Hence particle size analysis was carried out using standard sieve sets (# 12/16, 16/20, 20/30). The size analysis of different microcapsules (GG, and GG-PVA) showed that about 81 to 95 % were in the size mesh of – 16 +20. The size distribution of microspheres was found to be narrow in all the batches with an arithmetic mean size 1015.50 µm. The mean sizes of the major fraction of microspheres obtained were in the size range of 960-987 µm (Table 2). The size of microspheres was enhanced with increasing in the concentration of core: coat ratio. This could be due to greater amounts of coat material contained in a same volume of liquid droplet due to an increase in viscosity. Increase in concentration of glutaraldehyde has resulted slight increase in size of microcapsules (M7-M9) with a very narrow size distribution. Our results are in agreement with Aminabhavi et al [18]. Tween-80 was used to facilitate the stable dispersion of polymer in liquid paraffin with a fixed rotational speed. The stability of dispersion of particular polymer system depends on the concentration of emulsifier. The mean diameter of GG-PVA microcapsules (M10-M12) was found to range from 966-1000 µm (Table 2)with varying concentration of Tween-80 (% w/v) of medium. Increase in Tween-80 concentration has resulted decrease the mean size of microspheres. The optimal concentration Tween-80 was found to be 0.4 % w/v of medium.

3.4. Scanning electron microscopy

The morphological evaluation by scanning electron microscopy indicated that the prepared microcapsules of GG, and GG-PVA were discrete, almost spherical and completely covered with coat material(s). Figure.2a showed that, the outer surface of the GG microcapsules (M2) was smooth, free from crakes and granular deposits, indicating uniform distribution of the drug into the wall. The SEM photograph GG-PVA microcapsules (M4) (Figure 2b) showed that the surfaces of the microcapsules were rough with few deposits. The cross section of GG-PVA microcapsules (Figure.3) was made to observe internal structure. The section was dense with pores. The surface of GG-PVA microcapsules (M12) containing 0.4 % w/v Tween-80 (Figure 2c) was almost smooth with few pores.



(a)



(b)

(c)

Figure 2: SEM Photographs magnification 200X at 10kv a) GG drug-loaded microspheres (M2) b) GG-PVA drug loaded microspheres (M4) c) GG-PVA drug-loaded microspheres containing 4%w/v of Tween80(M12)

3.5. Drug content and encapsulation efficiency

The drug content of microspheres determines the amount of drug entrapped in the microcapsules. The drug content estimated in 50 mg of various microcapsules prepared with GG, and GG-PVA are shown in Table 2. The drug content was uniform and reproducible in each batch. It was decreased with increasing in the concentration of coating materials The encapsulation efficiency represents the percentage of entrapped drug with respect to total drug introduced into the polymer solution. The encapsulation efficiency was ranged from 81.30 to 94.24% irrespective of fabrication condition. Encapsulation was proportionate with the concentration of coat material(s). Increase in concentration of glutaraldehyde resulted decrease in encapsulation efficiency of GG-PVA microcapsules (M4-M6). Encapsulation efficiency was proportionate with concentration of Tween-80 and operating temperature. Conditions like 2.5 ml of glutaraldehyde, 0.4% w/v of Tween-80, were found to produce better GG-PVA microcapsules (M4) having encapsulation efficiency of 90.60% and good morphological characteristics.

3.6. Swelling studies

Swelling characteristic is related to the mucoadhesion and its environment. The swelling depends on the polymer concentration, ionic strength as well as presence of water [19]. During the dynamic process of mucoadhesion, maximum mucoadhesion *in vitro* occurs with optimum water content [20]. In order to obtain the data behavior of GG and GG-PVA microspheres during gastrointestinal passage, the swelling has been studied by incubating the microcapsules in pH 7.4 medium. Guar gum microcapsules (M1-M3) showed equilibrium swelling ratio (SR) 2.24, 2.48 and 2.76 respectively at the end of 4h. [Table 2] Increase in guar gum concentration resulted high SR values. The swelling studies of GG-PVA microcapsules showed equilibrium swelling ratio (SR) 2.80, 2.96 and 3.52 respectively at the end of 4h. (Table2) Microcapsules formulated by combination of GG and PVA resulted higher swellability than individual polymer. Overall studies showed that all microcapsules were rapidly swelled in pH 7.4 medium. The swelling was ranked GG-PVA > GG microcapsules. On other hand, the equilibrium swelling ratio of glutaraldehyde cross-linking microspheres (M7-M9) observed in the range 2.38, 1.74, and 1.54 at the end of 4h respectively (Table2). The results revealed that increasing in the concentration of cross-linking agent the SR values predominantly decreases. Glutaraldehyde causes cross linking by reacting with the hydroxyl groups of guar gum and PVA, thus interfering the free access of water to hydroxyl group of guar gum and PVA [21]. This significantly reduces the swelling rate of the microcapsules and consequently the penetration of the solvent into the microcapsules. Cross linking also reduces polymer chain mobility, increases glass transition temperature and decreases diffusivity [22]. The SR-values of microspheres with variable concentration of Tween80 (M10-M12) obtained in the range 2.53, 2.66, and 3.64 respectively (Table2). The concentration of surfactant increases SR value increases due relaxation of polymer net work in higher pH condition.

Table 2: Physicochemical characteristics of GG and GG-PVA microspheres

Formula Code	Mean Particle Size (μm)	Drug content (mg)		Microencapsulation efficiency (%)	$T_{50\%}$ (hrs)	Swelling ratio (%)
		Theoretical	Practical			
M1	966.41	33.33	28.50	85.50	3.4	2.24
M2	971.17	25.00	22.27	89.90	5.3	2.48
M3	978.06	20.00	18.36	91.80	6.6	2.76
M4	962.10	25.00	22.65	90.60	3.7	2.80
M5	980.24	25.00	22.85	91.80	5.5	2.96
M6	987.23	25.00	23.09	93.65	6.7	3.52
M7	960.46	25.00	23.06	92.24	3.5	2.38
M8	972.36	25.00	22.05	88.10	4.4	1.74
M9	986.49	25.00	21.35	86.00	5.2	1.54
M10	1000.92	25.00	23.60	94.40	3.3	2.54
M11	973.10	25.00	22.66	90.64	4.9	2.66
M12	966.43	25.00	21.16	84.64	5.6	3.64

3.7. In vitro mucoadhesion (wash off) test

The mucoadhesion is the phenomenon in which two materials, at least one of which is biological are held together by means of interfacial force [23]. The swelling behavior of polymers also influences the adhesion. The mucoadhesive property of microcapsules was determined by performing *in vitro* wash off test. The *in vitro* mucoadhesion data of selected microcapsules carried out with averted rat intestinal mucosa in presence of pH 7.4. Microcapsules prepared with GG and GG-PVA were found to adhere to intestinal mucosa over a period of 2 h.(Figure 3)The percent of mucoadhesion was proportionate with concentration of polymer in the microcapsules. The wash off was slow in case of microcapsules containing GG-PVA polymer as coat compared to that of guar gum. The order of percent of mucoadhesion was GG-PVA > GG microcapsules. The GG-PVA microspheres formulated with increasing concentration of surfactant observe less mucoadhesive property. The results indicated that the GG-PVA microcapsules show good mucoadhesive properties.

3.8. In vitro dissolution studies:

3.8.1. Effect of polymer concentration:

Glipizide release from different microcapsules (16/20) was studied in phosphate buffer of pH 7.4 as prescribed for glipizide tablets in USP XXIV for 12 h using dissolution test apparatus. In order to ascertain the influence of guar gum concentration on release of glipizide from microspheres (M1-M3) were found 84.30, 82.60, 78.60%w/w respectively at the end of 12 h.(Figure4) Their T_{50} values were found to be 3.4, 5.3 and 6.6 hrs.(Table 2). The release profiles clearly indicate that increase in the coat concentration resulted decrease in release rate. The retardation in the release rate was due to

thick polymeric coating of gaur gum and increase in diffusion path length through the polymer swelling when core: coat ratio increases.

To know the combined effect of GG and PVA concentration on drug release were studied for *in vitro* dissolution. The percent release of microcapsules of M4, M5, and M6 were found 93.10, 88.60, and 82.80 % respectively at the end of 12 h.(Figure 5) Their T_{50} values were found to be 3.7, 5.5, and 6.7 h.(Table 2) It was observed that high concentrations of coat composition (GG-PVA) resulted decrease in drug release rate. GG-PVA microcapsules M4 gave highest release rate with T_{90} of 9 hrs. Hence microcapsules formulated with 1:1, 1:1 polymer: copolymer ratio (M4) was selected for further characterization of effect of copolymer, cross linking, surfactant, plasticizer and operating temperature.

3.8.2. Effect of cross linking agent:

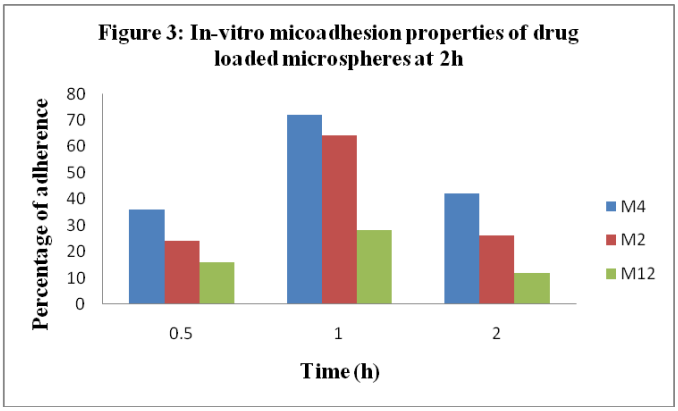
To understand the drug release from glipizide loaded GG-PVA interpenetrating network microcapsules were formulated with varied concentration glutaraldehyde (M7-M9) and were found 96.00, 93.10, 90.50, and 87.50 % at the end of 12h. (Figure 6) Thus the result exhibits a pronounced effect of extent of cross linking on the drug release profiles in all formulation. This may be due to the fact that the solvent uptake of these microcapsules decreases with increased cross linking. The percentage release data of GG-PVA cross linked microcapsules with 2 ml of glutaraldehyde was higher than those with high concentration of glutaraldehyde. The lowest percentage release values for GG-PVA microcapsules (M9) cross linked with 3.0 ml of glutaraldehyde was due to the rigidity of interpenetrating network polymer. GG-PVA microcapsules (M8) cross linked with 2.5 ml of glutaraldehyde was found good with respect to morphology and drug release potential.

3.8.3. Effect of surfactant

To ascertain the effect of surfactant on release profiles of GG-PVA microcapsules with varying concentration of Tween-80 from 0.1 0.2, 0.4% w/v of dispersion medium was used. The release rates of GG-PVA microcapsules (M10-M12) were found 84.00, 87.80, and 93.10% respectively at the end of 12 h.(Figure 7) The results showed that the release profiles were proportionate with surfactant concentration. GG-PVA microcapsules (M12) emulsified with 0.4% w/v of Tween-80 was found better with respect to release and morphological characteristics.

3.8.4. Comparison of commercial tablet

In vitro dissolution of commercial conventional tablet (Glynase 5mg) of glipizide was carried out as per adopted method. The commercial conventional tablet exhibited a fast release of 95% within 45 minutes. Our formulation M4 gave slow and spread release of 93% over a period 12 h. Hence GG-PVA microcapsules were found to be suitable carriers for controlled delivery of glipizide.



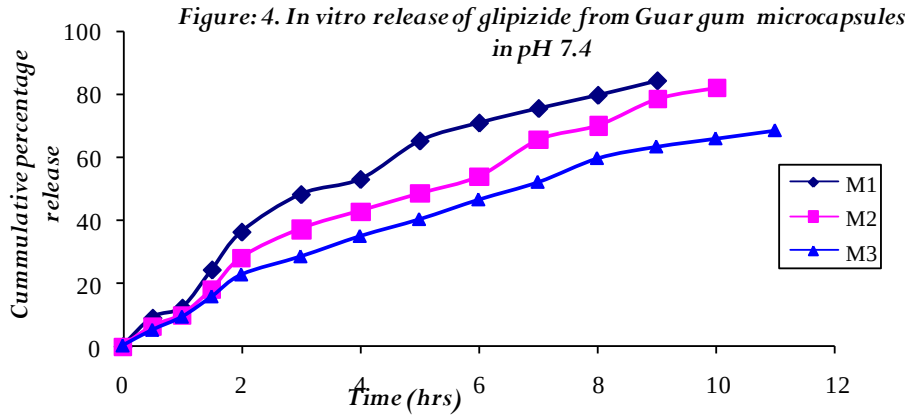


Figure 5 : In vitro release of glipizide from GG-PVA microspheres in pH 7.4

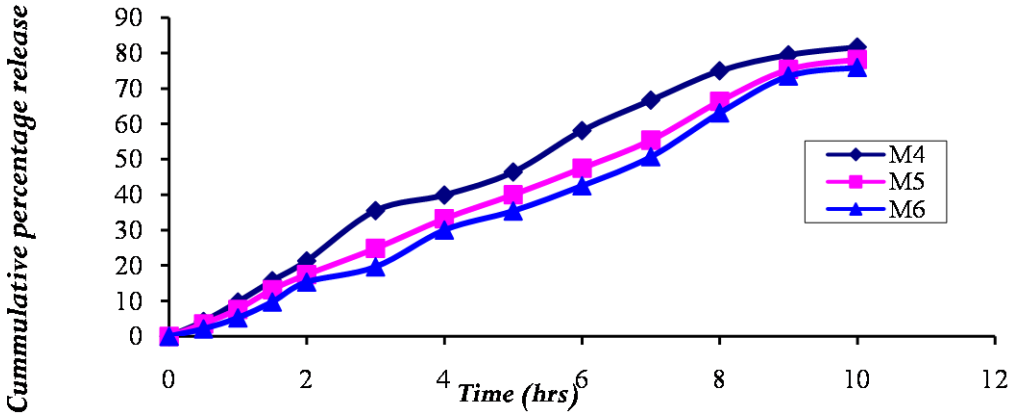


Figure 6:Effect of glutaraldehyde on release of glipizide from GG-PVA microcapsules in pH 7.4

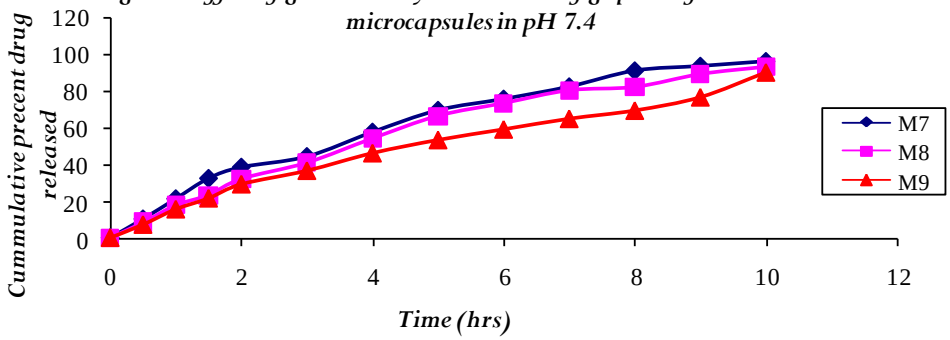
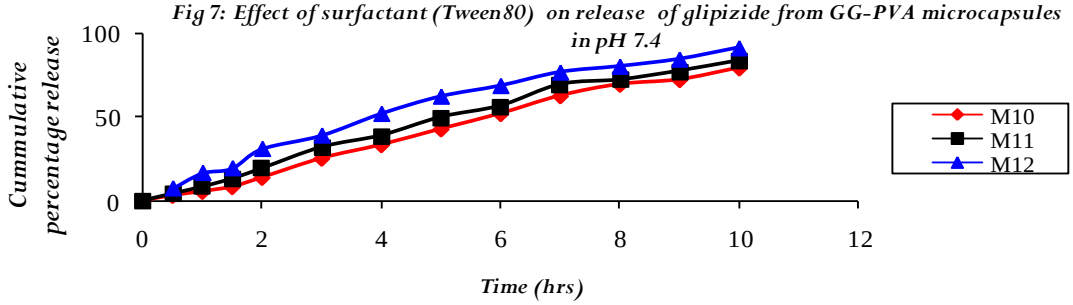


Fig 7: Effect of surfactant (Tween80) on release of glipizide from GG-PVA microcapsules in pH 7.4



3.8.5. Kinetics of drug release

Table 3 shows various drug release kinetic models representing Zero-order, First order, Higuchi's and Korsemeyer's equation on in-vitro drug release profiles of GG and GG-PVA microcapsules (M2 and M4) The interpretation of data was based on value of resulting regression co-efficient. When the data was plotted as per zero order kinetics fairly linear plots were obtained with their regression co-efficient values of 0.9886, and 0.9991 (M2, M4) the higher r value of 0.9991 indicates that the release of a drug from GG-PVA microcapsules (M4) was followed zero order kinetics [24]. Next the data was fitted according First order kinetics; linear plots were obtained with their regression co-efficient values of 0.9897, and 0.9906. Guar gum (M2) and GG-PVA microcapsules (M4) yielded high co-relation co-efficient values of 0.9897 and 0.9906 respectively indicating the order of release was as per First order equation[25]. Further the data was also plotted as per Higuchi's equation; a linear plots were obtained with their regression co-efficient values of 0.9843, 0.9889 for M2, and M4 indicating the mechanism of release from microcapsules was diffusion controlled [25]. Further, the data was plotted according Korsermeyer's equation. The plots showed linearity with their regression values of 0.9944 and 0.9882 with their respective slope values of 0.874, and 0.9525 for M2 and M4 Above observation led us to conclude that, the mechanism of release was diffusion controlled first order

kinetics for guar gum (M2) and GG-PVA (M4) microcapsules near to zero-order followed by swelling erosion of polymer network in the alkaline environment of GI-tract.

Table 3: Study of various kinetic models on In-vitro drug release of GG and GG-PVA microspheres of glipizide

Formulation Code	Zero-Order		First-Order		Higuchi's Matrix		Krosmeyer's-Peppas	
	n-values	r-Values	n-Values	r-values	n-Values	r-Values	n-Values	r-Values
M2	8.1457	0.9886	-0.0718	-0.9897	28.4226	0.9843	0.8746	0.9944
M4	8.0495	0.9986	-0.0650	-0.9796	27.2820	0.9658	0.9642	0.9958

4. CONCLUSION

Emulsification technique is very easy to prepare, free from any organic solvents and low manufacturing cost can be successfully used for preparation of glipizide microspheres using guar gum and PVA drug release modifier with high yield, spherical shape, uniform drug content and about 94%w/w entrapment efficiency. FTIR and DSC studies indicated no chemical reaction between drug and polymer(s). Swelling ratio and mucoadhesion of microcapsules were proportionate with concentration of polymer and coating polymer. Increase in concentration of coat material(s), and concentration of glutaraldehyde resulted decrease in release rate. The mechanism of drug release from GG microspheres was diffusion controlled followed by First order kinetics and whereas GG-PVA microcapsules approaching to Zero- order kinetics. Hence GG-PVA interpenetrating network microcapsules are found to be promising carriers for oral controlled delivery of glipizide.

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