Journal of Pharma Research
Available online through
www.jprinfo.com

Research Article
ISSN: 2319-5622

Development and evaluation of tizanidine hydrochloride loaded gum microspheres

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Received on: 03-076-2014; Revised and Accepted on: 21-07-2014

ABSTRACT

The objective of the present study was to developTizanidine Hydrochloride (TIZ) loaded into natural gum (Xanthan gum – XG & Guar gum – GG) and modified gum (Modified Guar gum – MGG) microspheres by emulsification solvent evaporation technique utilizing wetting agent. Effect of different process variables on drug loading studies during the preparation of microspheres was optimized. Sieve analysis data indicated that the prepared microspheres were in the range of 106 to 500 µm.SEM photomicrographs and sphericity factor confirms the prepared formulations are spherical in nature. DSC studies and FTIR spectra showed that the encapsulated drug was stable in the prepared formulations. Drug release from the prepared formulations were studied and compared with commercially available controlled release formulation Marketed product CR2mg controlled release capsule. It was observed that, there was no significant release of drug at gastric pH.

Keywords: *Natural and modified gum microspheres; Controlled release; Tizanidine Hydrochloride; Release kinetics; Pharmacokinetics, Bio Availability.*

INTRODUCTION

Controlled drug delivery is the most striking and challenging area in medical sciences, chemistry, materials science, pharmaceutics, and other biological sciences. Its application has resulted in the attainment of an improved quality of life and health care for human beings. A large number of natural gums are used to achieve oral Controlled drug delivery systems [1]. These natural gums according to their origin range from simple natural polymers to semi-synthetic and synthetic polymers. According to their nature, polymers are divided into hydrophilic and hydrophobic polymers [2]. However, to achieve and maintain the drug concentration within the therapeutic range, it is often obligatory to take the dosage form several times a day. This results in an undesirable see-saw pattern of drug levels in the body [3]. The growing interest in controlled release is because of its benefits like increase patience compliance due to reduced frequency of administration and less undesirable side effects.

Microencapsulation of drugs in a hydrophilic matrix such as natural gums, control the release of drugs [4]. The characteristics of microspheres containing drug should be correlated with the required therapeutic action and are dictated by the material and methods employed in the manufacture of delivery systems [5].The uniform distribution of theses multiple unit dosage forms along the gastro intestinal tract could result in more reproducible drug absorption and reduce risk of local irritation [6]. The selected hydrophilic and lipophilic drug for the present study have not been attempted by emulsification method in developingnatural and modified gums microspheres for oral controlled delivery systems [7], which highlighted the systematic study of the natural and modified gums microspheres [8] to develop controlled drug delivery systems.The natural gums used in the present study have good pharmaceutical and biological properties [9].Since dissolution is an important prerequisite for drug absorption in most of the acidic or basic drugs, the used carriers influence the drug absorption to the great extent [10].

Natural and modified gums have been used as drug carriers to achieve controlled drug delivery for the past few years.

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However natural and modified gums microspheres have gained a lot of interest owing to their versatile properties such as biodegradable, biocompatible and capacity to encapsulate hydrophilic drugs. Different natural and modified gums have been used as barrier coatings due to their hydrophilic nature [11].In the present study the following mentioned natural and modified gums have been used such as XG, GG & MGG. These natural and modified gums possess good pharmaceutical and biological properties and full fills few of the criteria mentioned above. The viscosity of XG solutions is increased in the presence of GG. This interaction is used synergistically in controlled release drug delivery systems [12]. Drug selected in present study was Tizanidine HCl.

MATERIALS AND METHODS

Materials:

Tizanidine HCl was obtained as a gift sample from EndocPharma, Gujarat. Xanthan Gum, Guar Gum and glutaraldehyde were procured from Loba chemicals, Mumbai. All nreagents used in present study were of analytical grade.

Methods:

Preparation of modified guar gum: [13]

Preparation of MGG was done by heating method. Powdered GG gum was taken in a porcelain bowl and subjected to heating using sand bath (1250C for 2h) for different time periods at different temperatures. The prepared modified form of GG was finally re-sieved (100 mesh) and stored in airtight container at 250C.

Swelling and water Retention capacity: [14]

The swelling and water retention capacity of the XG, GG and MGG were estimated by a slightly modified method. About 1.0 g of gum powder was accurately weighed and transferred to a 100ml stoppered measuring cylinder. The initial volume of the powder in the measuring cylinder was noted. The volume was made up to 100 ml mark with distilled water. The cylinder was stoppered and was shaken gently and set aside for 24 h. The volume occupied by the gum sediment was noted after 24 h. swelling capacity of the above gums were expressed in terms of swelling index as follows. Swelling index (SI) was expressed as a percentage and calculated according to the following equation:

$$SI = \left(\frac{Vf - Vo}{Vo}\right) \times 100 \quad \text{---------- 1}$$

Where, Xo is the initial height of the powder in graduated cylinder and Xt denotes the height occupied by swollen gum after 24h. The contents from the measuring cylinder from the above test were filtered through muslin cloth and the water was allowed to drain completely into a dry 100 ml graduated cylinder. The volume of water collected was noted and the difference between original volume of the mucilage and the volume drained was taken as water retained by the sample referred as water retention capacity or water absorption capacity of the polysaccharide.

Viscosity measurement:

The viscosity of 1% (w/v) XG, GG and MGG solutions were measured according to the USP XXX, NF XXIV, at 370C using Brookfield, DV-II+ pro viscometer and spindle 52 (LV2).

Preparation of microspheres:

Blank (Drug-free) and drug loaded microspheres were prepared by water-in-oil (W/O) emulsification solvent evaporation technique. Microspheres were prepared by using different ratios of drug: natural gum at different ratio (1:1:05, 1:1:0.75, 1:1:1) presented in **Table 1**. Gums were allowed tohydrate in 20 ml water for3 hours to achieve a viscoussolution. Weighed quantity of drug (1gm) previously passed through sieve No. 100 was dispersed in 10 ml of methylene chloride and dissolved in each aqueous solution of gums. The above drug-gum dispersion was acidulated with 0.5 ml of concentrated sulphuric acid to give a clear viscous solution. The resultant solution was emulsified into the oily phase by poured into 200 ml of paraffin liquid containing 0.5 % span 80 as an emulsifying agent. Stirred mechanically at 1800 rpm for 210 min using a stirrer and heated by a hot plate at 50 °C. 1.2 % w/v dichloromethane was added as encapsulating agent and 0.15 % w/v of glutaraldehyde as cross linking agent, stirring and heating were maintained for 2.5 hr until the aqueous phase was completely removed by evaporation. The oil was decanted and collected microspheres were was hed with water to remove surfactant residue and three times with 100 ml aliquots of n-hexane, filtered through whatman filter paper, dried in an oven at 80 °C for 2 hrto collect discrete, solid, free flowing microspheres and stored in a desiccators at room temperature. Formulation was showed in **Table 1**.

Table No. 1: Code for the prepared natural and modified gums microspheres formulations loaded With Tizanidine hydrochloride

Formulations	Drug	Xanthan Gum	Guar Gum	Modified Guar Gum
TXG1	1.0	1.0	0.5	-
TXG2	1.0	1.0	0.75	-
TXG3	1.0	1.0	1.0	-
TXMG1	1.0	1.0	-	0.5
TXMG2	1.0	1.0	-	0.75
TXMG3	1.0	1.0	-	1.0

T=Tizanidine hydrochloride, X = Xanthan Gum, G = Guar Gum, MG = Modified Guar Gum

Differential Scanning Calorimetry (DSC):

All dynamic DSC studies were carried out to pure drug (Tizanidine hydrochloride) and for microspheres with and without drug on Du Pont thermal analyzer with DSC-60 module. Calorimetric measurements were made with empty cell (high purity alpha alumina discs were used for Tizanidine hydrochloride of Du Pont Company) as the reference. The instrument was calibrated using high purityindium metal as standard. The dynamic scans were taken in nitrogen atmosphere at heating rate of 100c/min. the runs were made in triplicate.

Fourier Transform Infrared radiation measurements (FT-IR):

FTIR analysis was carried out for pure drug (Tizanidine hydrochloride) and for microspheres with and without drug using KBr pellet method on FTIR spectrophotometry type schimadzu model 8400S, USA.

Scanning electronic microscope (SEM) study:

SEM photographs were taken with a scanning electron microscope model Joel-LV-5600, USA, at the required magnification at room temperature. The photographs were observed for morphological characteristics and to confirm special spherical nature of the microspheres.

Micromeritic Properties:

Micromeritic properties such as tap density, Carr index,angle of repose were calculated. Tap density of the pre-pared microspheres was determined using tap density testerand percentage Carr index (%CI) was calculated. Angle ofrepose (θ) was assessed to know the flow ability of themicrospheres, by a fixed funnel method [15].

Drug Loading and Encapsulation Efficiency:

10mg of microspheres was dispersed in 10ml of phosphate buffer. The sample was ultra-sonicated for 3 consecutive periods of 5min. Solution was filtered and from the filtrate obtained, 1ml of solution was transferred to 10ml volumetric flask and diluted up to the mark. The drug content was calculated by using the formula:

$$\text{Amount of drug} = \frac{\text{conc.from standard graph} \times \text{dilution factor}}{1000} \quad \text{----- (2)}$$

Percent drug loading and encapsulation efficiency were calculated using the following equations:

$$\%\ drug\ loading = \frac{weight\ of\ drug}{weight\ of\ microparticles} \times 100 \quad \text{------- (3)}$$

$$Encapsulation\ efficacy = \frac{actual\ drug\ content}{theoretical\ drug\ content} \times 100 \quad \text{---- (4)}$$

In vitro studies:

Dissolution studies were carried out for all the batches of the prepared formulation (6 batches) and their corresponding commercial formulations, the details of which are given in **Table 2**.

Table No. 2: Dissolution media used for the prepared formulation (6 batches) and their corresponding commercial formulations

S. No.	Formulations	Quantity used	Dissolution media	
			For 2 h	For 10 hrs
1	Tizanidine hydrochloride (TIZ)	Equivalent to 2 mg of TIZ	pH1.2 HCL buffer	pH 6.8 phosphate buffer
2	Marketed product	Tablet containing 2 mg of TIZ	pH1.2 HCL buffer	pH 6.8 phosphate buffer

Automated dissolution tester USP XXI (TDL 08L) type II apparatus was employed in the present studies. The dissolution media was maintained at 37 °C ±0.5 °C and stirred at 100 rpm. Drug release from the formulations were determined by with drawl of 5ml samples using guarded pipette at 30min interval for the firstsix hours and one interval for the remaining six hours. Samples were estimated after appropriate dilution. Release studies were carried out in triplicate.

Stability Studies of the Optimized Formulation:

Optimized formulation of the microspheres was selected for stability studies (ICH Quality Guidelines, 2003) according to ICH guidelines by storing at 25°C/60% RH and 40°C/75% RH for 90 days. Samples were withdrawn on the 15th, 45th and 90th days and checked for changes in physical appearance and drug content.

RESULTS AND DISCUSSION

Swelling, viscosity and water retention:

The results of viscosity studies showed in table 3revealed that the viscosity of GG was found more than the XG and modified forms. MGG showed little more viscosity than GG. The results indicated that the viscosity of GG markedly higher than MGG. From this we can conclude that GG poses more viscous nature (GG > XG >

MGG). Swelling is an indicative parameter for rapid availability of drug solution for diffusion with greater flux. Upon exposure to GIT fluids, the carboxylic group becomes ionized leading to repulsion between similar charges along with increase in osmotic pressure and hence favored swelling [16]. Swelling data revealed the amount of gums and their modified forms played important roles in solvent transfer. The result shown in table 3 indicated that with an increase in polymer concentration, the degree of swelling also increased. The swelling studies of the GG, MGG & XG possessed swelling properties similar and not reduced significantly. Due to the swelling nature of the gums, the extensivesurface of carrier is increased during dissolution and dissolution rate of deposited drug is markedly enhanced. Water retention capacity of gums is the amount of water retained in it that indicates ability of carrier towards hydrophilic nature .The water retention capacity of GG found to be more than XG, MGG [17].

Table No. 3: Viscosity, swelling studies & water retention capacity of XG, GG & MGG

Product	Viscosity * (CPS)	Swelling Index* (%)	Water retention capacity* (ml)
XG	1423 ± 16	25.87 ± 3	18.03 ± 3.02
GG	4392 ± 14	25.98 ± 3	26.12 ± 3.01
MGG	1603 ± 23	24.92 ± 2	20.32 ± 2.09

*Standard deviation n = 3

Differential Scanning Calorimetry (DSC):

In order to study any possible interactions between the drug and polymers, DSC studies were carried out. The DSC thermo grams obtained are reported in **Fig. 1**. From the thermo grams it was observed that, TIZ displayed a single sharp peak at 291.56 °C corresponding to its melting point and Formulation TXMG2 showed peak at 279 °C. Hence it can be observed that there was no significant interaction between the drug and polymers used.

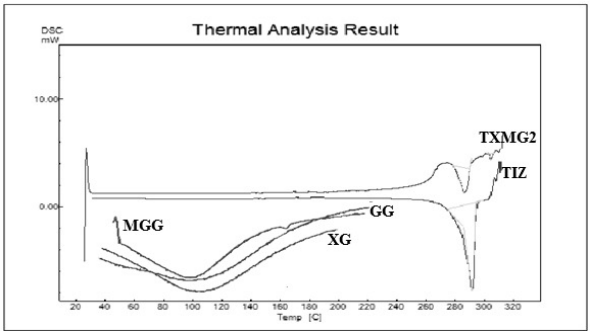

Fig. 1: DSC thermograms of TIZ, XG, GG, MGG and TXMG2.TXMG2- Tizanidine loaded gum microspheres, TIZ- Tizanidine hydrochloride, XG-Xanthan gum, GG- guar gum, MGG- modified guar gum.

Fourier Transformed Infrared (FT-IR) Spectroscopic Analysis:

Tizanidine hydrochloride pure drug and the optimized formulation (TXMG2) were subjected for FT-IR spectroscopic analysis for compatibility studies and to ascertain whether there was any interaction between the drug and the polymers used. The IR spectra of Tizanidine Hcl and optimized formulation (TXMG2) were found to be identical as presented in **Fig. 2**. The characteristic IR absorption peaks of Tizanidine at 3248.08 cm^{-1}(N-H bend, primary amine group), 2364.32 cm^{-1}(carboxylic acids, OH bond), 3074.88 cm^{-1} (aromatic C-H stretch), 1654.01 cm^{-1}(C=C stretch), 674.38 cm^{-1} (C-H stretch) were present in both pure drug and Formulation (TXMG2). The data is tabulated in **Table 4**. FT-IR spectra of the optimized showed all the Tizanidine characteristic absorption bands with minor fluctuations suggesting the absence of interactions between the drug and other components of formulation.

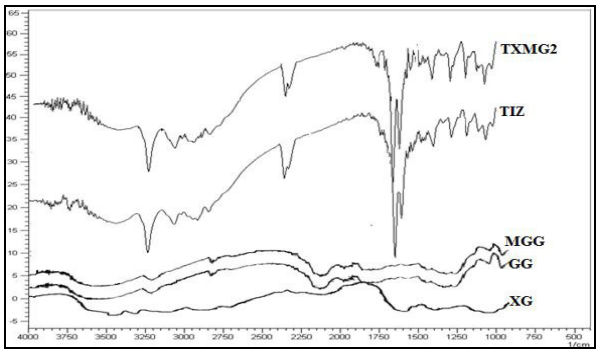

Fig. 2: FTIR spectra of Pure TIZ, TXMG2, XG, GG and MGG. TXMG2- Tizanidine loaded gum microspheres, TIZ- Tizanidine hydrochloride, XG- Xanthan gum, GG- guar gum MGG- modified guar gum.

Table No. 4: FT-IR data for pure drug and formulation (TXMG2)

Group absorption	Frequency of pure drug (in cm-1)	Frequency of formulation (in cm-1)
N-H Stretching	3248.08	3245.82
O-H Bending (carboxylic acid)	2364.32	2353.60
C-H Bending (aromatic)	3074.88	3074.88
C-H Stretching	674.38	674.36
C=C Stretching	1654.01	1649.67

SEM:

The scanning electron micrographic photographs (SEM) were obtained to identify the morphology of the prepared microspheres. The SEM photo micrographsTXMG2 (**Fig. 3**) showed that the prepared microspheres were spherical, solid, discrete, free flowing in nature and had a smooth surface. The presence of cross linking agent appears to favor the formation of rigid and tight network and hence spherical free flowing microspheres were obtained [19].

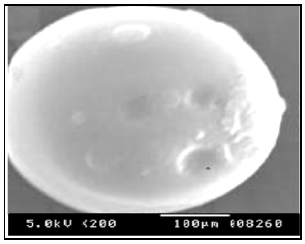

Fig. 3: SEM photographs of microsphere

Micromeritic properties:

Generally the microparticulate drug delivery systems are formulated as single unit dosage forms in the form of capsule or tablet. Such microparticulate systems should possess the required and better Micromeritic properties. The flow property of the wax/fat microspheres was studied by calculating the angle of repose θ and % Compressibility index, I. The values of θ0 ranged between 23.250 to 24.880 for TIZ loaded microspheres presented in **Table 6**. From the data in **Table 6** indicating θ0 values were well within the limit and indicating reasonably good flow potentials for the prepared microspheres. The values of Carr's index were found to be 10.12 % to14.55% for TIZ loaded microspheres. It shows that the % compressibility index values were well within thelimit and good flow characteristics of the microspheres. The values of Tapped density for TIZ loaded microspheres ranged between 0.3 to 0.5 g/cm^3, presented in **Table 5**. Density difference between the formulations is negligible and the density values of the formulations were well within the limit, indicating the prepared microspheres were non aggregated and spherical in nature.

Table No. 5: Micromeritic properties of the TIZ loaded microspheres

Formulation	Average size (µm) Mean ± SD*	Angle of repose (θ0)	Tapped density (g/cm3)	Carr's index (%)
TXG1	406 ± 03	24.54±0.92	0.4 ± 0.64	10.53±0.74
TXG2	421 ± 01	23.42±0.25	0.5 ± 0.92	11.59±0.85
TXG3	456 ± 02	23.45±0.88	0.4 ± 0.43	12.56±0.46
TXMG1	361 ± 04	24.30±0.65	0.3 ± 0.01	13.54±0.89
TXMG2	372 ± 03	23.25±0.46	0.5 ± 0.55	12.62±0.65
TXMG3	383 ± 02	24.98±0.74	0.4 ± 0.82	11.59±0.78

*Standard deviation n = 3

Drug Loading and Encapsulation efficacy:

The percent of drug loading in the TIZ loaded formulations were in the range of 20.17 % to 22.98 %. A significant variation in the drug amount to microspheres size was observed indicating that the ratio between the drug and gums used and as the ratio of gum increases drug loading was found to be increases. It was found that the TIZ loaded MGG microspheres showed little higher drug loading than GG microspheres. The encapsulation efficiency (%) was found to be more for TXMG1 (86.02 %) microspheres when compared to TXG1 (86.89 %) and it can be concluded that the microspheres TXMG2 have more encapsulation efficiency. It was observed that rapid evaporation, fast solidification of the microspheres and also high solubility of Dichloromethane, which might account higher loading of drug. This might be due to increased relative surface area of the microspheres20. Results were showed in **Table 6**.

Table No. 6: Drug loading properties of TIZ loaded microspheres

Formulation	Loading (%) Mean ± SD*	Encapsulation Efficiency (%) Mean ± SD*
TXG1	20.17 ± 0.26	86.89 ± 1.32
TXG2	21.13 ± 0.27	87.83 ± 1.30
TXG3	21.67 ±0.43	88.19 ± 1.40
TXMG1	20.98 ± 0.19	86.02 ± 1.08
TXMG2	22.98 ± 0.28	88.16 ± 1.61
TXMG3	21.43 ± 0.41	87.68 ± 1.50

*Standard deviation n = 3

***In Vitro* Drug Release:**

Dissolution studies were carried out at pH 1.2 HCl buffer for 2 hours followed by pH 6.8 Phosphate buffer for 10 h using XXI dissolution apparatus Type II. The dissolution time profile is recorded in **Fig. 4** TIZ microspheres for Marketed productCR - 2mg. From the release studies it was observed that there is a small amount of drug was release at gastric pH from TIZ loaded microspheres. But drug was released in the biphasic manner consisting of initial burst release stage followed by a slow release at intestinal pH from TIZ loaded microspheres. At the end of 12th hour, drug release in the intestinal environment for the TIZ loaded microspheres ranges from 82.4 % to 92.3 % .For the Marketed productCR- 2mg it was 96.5%. The in vitro drug release considerably retarded from the TIZ loaded microspheres when compared with Marketed productCR– 2mg. It was observed that as the polymer to drug ratio increases the drug release was found to be decreases. More amount of TIZ released from formulation TXMG2 than other formulations. Microspheres prepared with MGG exhibits more drug release. Increase in dissolution rate of TIZ from MGG was found to be greater. ANOVA ($P < 0.005$) demonstrated that the differences were statistically significant. Due to hydrophilic nature of the carrier hydrodynamic microenvironment around the particles was changed. During the process of drug dissolution from ordered mixtures of hydrophilic drug (TIZ) and hydrophilic carriers, when a drug & carrier particle come in contact with the dissolution fluid, seeping of dissolution medium into the drug & carrier particle takes place, which initiates the formation of stagnant gel layer of carrier around the particles.

It was observed that as the concentrations of gum increases the drug release was found to be less. TIZ loaded MGG microspheres showed better drug releasethan TIZ loaded GG microspheres. The viscosity of 1% W/V solution of MGG was 1603cps, which is about 3 times lower than that of GG [20]. Hence, the dissolution rate of TIZ was observed low, microspheres prepared with GG, though the physical state of the drug is identical in the mixture of GG with respect to mixture of MGG. Here XG was used as common gum to all the microspheres formulation to synergize the viscosity and hence to control the drug release. It was observed that GG & MGG are more viscous resulting in formation of agglomerates of drug and carrier particles during dissolution. Formed agglomerates failed disperse easily in the dissolution medium, so that drug release was observed slow. During the dissolution process, formed agglomerates of drug and carrier particles from GG are dispersed rapidly throughout the dissolution medium than the MGG agglomerates. So that the formed agglomerates expose a greater surface area, resulting in rapid drug release. This factor also contributed to the significant difference between the dissolution rates of GG and MGG. This typical drug release behavior was commonly observed in diffusion controlled drug delivery systems [21].

It could be seen that increasing the polymer concentration level from 0.5, 0.75 &1.0 % caused significant reduction in the drug release. A controlled release of drug from the MGG microspheres than GG microspheres was observed and can be attributed to the viscous hydrophilic barrier limiting access of water and dissolution of drug. Kiortsis S et al [22] explained the drug release from dosage form comprising of cellulosic structure by three steps. Firstly, the penetration of the dissolution media into the dosage forms by hydration. Secondly, the erosion of the matrix and thirdly, transport of the dissolved drug either through the hydrated matrix or fromthe parts of the eroded area of dosage forms to the surrounding dissolution medium. It was found that as the concentration of gum increases, slower penetration of dissolution medium in the matrices and the drug release decreases. It was observed that for all the formulation the rate and extent of drug release is decreases with increase in the concentration of the gums and their modified form. The difference in the mean of % drug release between batch series was significant ($p<0.05$). From the above observation formulation TXMG2 was identified as an ideal formulation based on its physicochemical and release characteristics.

The observed profile of the release TIZ from microspheres were compared with those obtained from an equivalent amount of Marketed productCR- 2mg. The prepared TIZ microspheres have considerably retarded the drug release when compared to encapsulated commercial formulation. Exhaustion of drug from microspheres occurred in about 14 to 16 hours as obtained by extrapolation of the kinetics results. The drug release performance was greatly affected by the material use in the microencapsulation process.

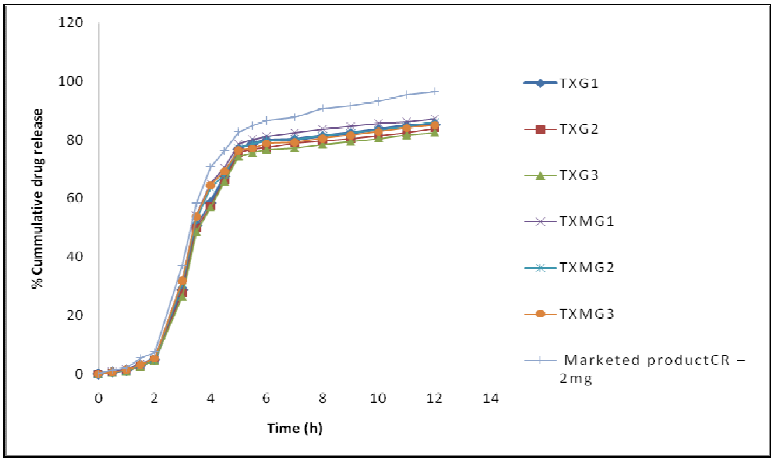

Fig. 4: Dissolution time data for TIZ loaded microspheres and Marketed productCR – 2mg

Stability studies:

Many factors, combined with microspheres composition, the parameters used in the preparation method and microspheres storage conditions, may affect the stability of microspheres. Therefore, in most cases, it is difficult to identify specific determinants and the behaviors observed are the consequences of combinations that necessarily lead to general conclusions.

The objective of stability studies was to predict the shelf life of a product by accelerating the rate of decomposition, preferably by increasing the temperatureand RH. The stability studies for TXMG2 were carried out for 90 days. These samples were analyzed and checked for drug content at regular intervals. The obtained data is presented in **Table 7**. From the data it was observed that the formulation did not undergo any significant changes in the drug content during the study period.

Table No. 7: Drug content estimation after stability studies from formulation TXMG2

Stability Condition	Sampling (in days)	Drug content (in %) Mean ± SD*
250 C/ 60% RH	0	99.70 ± 0.43
	15	99.66±0.17
	45	99.65±0.23
	90	99.51±0.18
30°C / 65% RH	0	99.70 ± 0.43
	15	99.47±0.24
	45	99.39±0.36
	90	99.25±0.12
40°C/ 75% RH	0	99.70 ± 0.43
	15	99.57±0.76
	45	99.43±0.44
	90	99.13±0.24

Summary and conclusion:

These Tizanidine loaded gum microspheres were prepared by water-in-oil (W/O) emulsification solvent evaporation technique using different ratios. The prepared microspheres were characterized by FT-IR analysis, DSC analysis, SEM analysis and particle size analysis. They were evaluated for drug loading, percentage yield, encapsulation efficiency, dug content, in vitro drug release, in vivo studies and stability studies.

The optimized phase concentration for preparing microspheres was TXMG2(1:1: 0.75), which was used to avoid aggregation of microspheres.It was found that span 80 having HLB value (hydrophilic lipophilic balance) 4.3 were found to be more suitable to increase substantial dispersion of drug in XG,GG and MGG.It was found that 0.5% w/w of glutaraldehyde was used as a cross linking agentto cross link the microspheres.It was found that 1.2 % w/v Dichloromethane as drug loading solvent providedthe best loading for drug.The microspheres prepared were characterized for size distribution and particle size was in the range of 106 µm to 500 µm and 59.1% to 63.5% were of sized fraction 250 µm and 314µm to 456 µm respectively. From the SEM studies it was observed that microspheres are spherical and smooth surface. FT-IR studies indicated that there was no interaction between the polymers and the drug in the formulation, as the principle peaks of the drug and formulation were not altered. From the DSC thermo grams, it was evident that the decomposition temperatures of both the drug and formulation are closer; hence no significance interactions exist between the drug and polymers. The results obtained from the drug entrapment efficiency showed that the drugwas uniformly distributed in all the prepared formulations. The in vitro drug release was found to be controlled up to 12 hours for the formulation (TXMG2). Hence it can be concluded that modified guar gum microspheres may be useful in controlling the drug release. The results of mathematical model fitting of data obtained indicated that, the best-fit model in all the cases was found to be Peppa's model. The result of stability studies carried out on the optimized formulation, TXMG2 indicated that after 90 days there was no significant change in the drug content when stored at accelerated storage conditions i.e., 40° ± 2°C/ 75 ± 5% RH.

From the above results it can be concluded that GG and MGG can be successfully utilized for the preparation of microspheres and can be used for the improved delivery of poorly water soluble drugs.

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How to cite this article:

Nawaz Mahammed et al.,: Development and evaluation of tizanidine hydrochloride loaded gum microspheres. J. Pharm. Res., 2014; 3(7): 116-121.

Conflict of interest: The authors have declared that no conflict of interest exists.

Source of support: Nil