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PREPARATION AND EVALUATION OF CONTROLLED RELEASE MATRIX TABLETS OF METFORMIN HYDROCHLORIDE BY USING *LANNEA COROMANDELICA* PLANT GUM AND OTHER POLYMERS

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ABSTRACT

The study was aimed for developing controlled release matrix tablets of highly water-soluble Metformin hydrochloride by wet granulation method using *Lannea coromandelica* plant gum, hydroxypropylmethylcellulose (HPMC) and xanthane gum as polymers. The flow properties of blended powders, crushing strength, friability, swelling index and drug content uniformity of compressed tablets were determined. *In vitro* drug release studies of the matrix tablets were conducted in simulated gastric fluid (pH 1.2), simulated intestinal fluid (pH 6.8) and the kinetics of drug release was determined by fitting the release data to different kinetic models. *Lannea coromandelica* plant gum was found to be best suitable for wet granulation method, having a good compressibility index value of less than 20. The metformin hydrochloride matrix tablets produced generally possessed fairly good physical properties. Tablet swelling and drug release in aqueous medium were dependent on the type and amount of release retarding polymer and the solubility of drug used. Controlled release of metformin from the matrix tablets in aqueous medium was achieved by selected polymers. Drug release from metformin hydrochloride tablets fitted to zero order, first order and Higuchi model. The drug release mechanisms from the matrix tablets were found to be linear with all the matrix tablets with correlation coefficient (r^2) values > 0.956. When the release pattern data were analysed as per the Peppas equation, the release exponent (n) was in the range of 0.241-0.444 in the all matrix tablets indicating that the release mechanism from these matrix tablets were by Fickian diffusion. Hence, it can be concluded that, the use of natural polymers in novel drug delivery systems play a significant role when compared with synthetic polymers and found to be economic.

INTRODUCTION

Natural polymers play a significant role in the formulation and development of a new controlled release dosage forms. In recent years, natural polymers utilization was growing rapidly and it continues process and important in the new formulation development of the controlled released dosage forms[1]. Therefore, they needs a novel approach to enhance the use of natural polymers in the formulation development of controlled release dosage form, because of the ease of availability at an affordable price, high safety margin and higher productivity[1-3]. Metformin Hcl is an oral hypoglycemic agent, which belongs to the class of biguanides[4, 5] and widely used in the management of type 2 diabetes. The oral bioavailability of metformin HCl is about 60.9%.

MATERIALS AND METHODS:

Metformin Hydrochloride obtained as a gift sample from Reddy Labs (Hyderabad, India). *Lannea coromandelica* gum was procured punyagiri hills, S.Kota, Visakhapatnam district, A.P. Xanthan gum, HPMC was obtained Delta scientific, Vijayawada. All other ingredients like lactose, talc and magnesium stearate used were of analytical grade, and procured from commercial vendors.

METHOD

Drug-excipient compatibility studies:

Assessment of possible incompatibilities checked out between the drug substance and different excipients used in the formulaton. An important part of pre-formulation studies required during the development of solid dosage forms. Therefore, the pure drug and the other additives in the formulations were subjected to infra-red (IR) studies.

Fourier Transform Infrared (FTIR) spectral analysis[6, 7] The compatibility of the drug with other excipients used under experimental condition were studied. The study was performed by taking pure drug sample in KBr pallets (Perkin Elmer, spectrum-100, Japan). The scanning range was 400 to 4000 cm-1 and the resolution was 1cm-1. The spectral analysis was used to check the compatibility of drug with other excipients used.

Preformulation studies

Micromeritic properties: Angle of repose, bulk density and tapped density, compressibility index, carr's index and hausner's ratio were determined for prepared granules[8, 9, 10.]

Preparation of metformin Hcl matrix tablets[11, 12]

Matrix tablets, each containing 500 mg of metformin HCl were prepared by wet granulation technique. The compositions of various formulations of the tablets with their codes are listed in Table 2. The ingredients were passed through a 12-mesh sieve. A blend of all ingredients except glidant and lubricant was mixed, a particular attention had been given to ensure thorough mixing and phase homogenization. Granulation was done manually with distilled water as granulating fluid. The wet masses were passed through a 16 mesh sieve and the wet granules produced were first air dried for 15 min. The dried granules were sized by a 16-mesh sieve and after adding lubricating agent and magnesium stearate (glidant), compression was carried out using 14 mm flat faced circular punches for getting tablets on an eight station rotary press tablet compression machine (Rimek Minipress, Ahmadabad, India) at a constant compression force. All the tablets were stored in airtight containers for further study. Prior to compression, the granules were evaluated for their flow and compressibility characteristics.

Evaluation of physical properties of matrix tablets:

Hardness test: The hardness of the metformin Hcl matrix tablets was determined with a monsanto tablet hardness tester. Ten tablets were used in each test and the mean hardness was calculated [13].

$$Mean\ Hardness = \frac{Total\ hardness\ of\ 10\ tablets}{10}$$

Friability test: The friability of the metformin Hcl matrix tablets was evaluated with a roche friabilator. Twenty tablets were weighed prior to placing them in the friabilator chamber and at the end of the test, their weight was again recorded. Finally, the loss in weight was calculated [13].

$$\%\ Friability = \frac{Initial\ weight - Final\ weight}{Initial\ weight} \times 100$$

Weight uniformity: For weight uniformity test, twenty metformin Hcl matrix tablets were randomly selected and weighed using an electronic weight balance and weight variation (%) was calculated.

Drug content determination: Twenty metformin Hcl matrix tablets were weighed and finely powdered. An amount of tablet powder equivalent to 50 mg of metformin Hcl was accurately weighed

and transferred to a 50 mL volumetric flask and 50 mL of SGF without enzyme was added. The solution was subjected to sonication for 10 min for complete extraction of metformin Hcl and the solution was made up to the mark with the medium (SGF without enzyme) to obtain a concentration of 1 mg/mL. The above solution was diluted using the medium to get a concentration of 100µg/mL and the absorbance was measured by UV Spectrophotometrically at 234 nm. The actual concentration of the sample was determined from the standard calibration curve of Metformin Hcl.

***In-vitro* dissolution studies for matrix tablets[14]**

The releases of metformin Hcl from matrix tablets were determined using USP basket type tablet Dissolution Tester apparatus. Dissolution test was performed at 100 rpm using 900 mL of SGF without enzyme for first 2 h followed by SIF up to 24 h. The temperature was maintained at 37 ± 0.2°C. Samples each containing 5 mL were withdrawn at 1, 2, 4, 6, 8, 10, 12, 14, 16, 20 and 24 h time interval, filtered through a Whatman filter of 0.45 µm size and replaced with an equal amount of fresh dissolution medium to maintain sink condition. Samples were then suitably diluted and analyzed for drug content spectrophotometrically at 234 nm. The release studies were conducted in triplicate**.**

Kinetics of *in-vitro* drug release: To study the release kinetics *in-vitro* release data obtained was applied to kinetic models such as zero-order, first order, Higuchi and Korsemeyer-Peppas.

RESULTS AND DISCUSSION

Compatibility study: Spectra of the pure drug, physical mixture of drug and excipient were recorded in between 400-4000 wave number (cm-1).

$$Weight\ uniformity = \frac{Average\ weight - Individual\ weight}{Average\ weight}$$

The FTIR spectral analysis showed that there is no appearance or disappearance of any characteristic peaks of pure drug metformin Hcl and in the physical mixture which confirms the absence of chemical interaction between drug and polymers. The results are shown in Table 3.

Micromeretic properties: Granules of all the formulations were subjected to various pre-compressional evaluations such as angle of repose, compressibility index, hausner's ratio, granular friability index, compactibility, cohesiveness and kawakita analysis. Results of all the pre-compressional parameters performed on granules are shown in Table 4 and 5. The angle of repose was found to be ranging from 22º.12±1.1 to 25º.98±0.4 for the granules of all the formulations. Compressibility index was found to be ranging from 15.02±0.02 to 20.05±0.5 % for the granules of all the formulations. The results of Hausner's ratio were found to be lesser than 1.21 which indicates better flow properties. The results of angle of repose (<30) indicates good flow properties of the grnules. This was further supported by lower compressibility index values. Generally compressibility values up to 15% results in good to excellent flow properties.

Evaluation of matrix tablets: All the batches were produced under similar conditions to avoid processing variables. The matrix tablets of metformin Hcl were prepared with xanthan gum, HPMC 100 cps and *Lannea coromandelica* gum at various drug to polymer ratios as mentioned earlier. Higher drug content found (94.91 to 98.41%) for all matrix tablets indicated uniform mixing of drug with polymers and other excipients. The hardness of the tablets was in the range of 4.60 to 5.61 kg/cm^2 indicating that the prepared tablets were mechanically stable and the selected polymers have good binding property. Friability values were in the range of 0.24 % - 0.54 %, which ensures loss of material from the surface or edge of tablets was within the permissible limit and it also suggests good handling properties. All the formulations passed

weight variation test which is an indicative of good flowability. The values are shown in Table 4.

***In-vitro* dissolution studies from matrix tablets:** The drug release rate was found to be decreasing as the concentration of polymer increased. Formulation F19, F20 and F21 were able to sustain the release up to 14, 16 and 24 h respectively (Figure 11). In this case, metformin Hcl is a water soluble drug which allows quicker penetration of dissolution fluid into the matrix tablet, resulting in quicker release of drug and therefore large amount of polymer was required to sustain the release for 24 h. On increasing the proportion of xanthan gum prolonged release was achieved up to 24 h. Tablets made up of xanthan gum based granules showed penetration of the medium into the core followed by swelling of the structure. Xanthan gum, the control release agent included in the formulations, is known to have the ability to hydrate very rapidly in addition to exhibit swelling [15]. It is speculated that the drug release from matrix tablets made of xanthan gum based granules was a result of hydration of the gum, which swelled extensively forming a barrier through which drug diffused. Erosion of the tablets was probably an important mechanism of drug release since gradual loss of size of the swollen tablets was noticed by visual inspection during dissolution. Formulation F21 was selected as the best formulation keeping in view the minimum amount of xanthan gum required for sustaining the release up to a period of 24 h. The release rate of drug was found to be decreasing as the concentration of HPMC 100 cps increased. Formulation F22, F23 and F24 were able to sustain the release up to 12, 14 and 24 h respectively. The reason for this can be attributed to the formation of a stronger gel layer around the tablet, with few interstitial spaces between the microgels [16]. Drug release decreased with increase of polymer loading as HPMC polymers form viscous gelatinous layer (gel layer) upon exposure to aqueous medium by undergoing rapid hydration and chain relaxation and this gel layer acts as the barrier to release drug and as a result the drug release was prolonged. This may be the reason that HPMC 100 cps in the present ratio was not sufficient to sustain the release beyond 14 h. The release rate was found to be decreasing as the concentration of polymer increased. Formulation F25, F26 and F27 were able to sustain the release up to 12, 16 and 24 h respectively. Formulation F25 showed an initial burst release with sustain release for 12 h. On increasing the proportion of *Lannea coromandelica* gum rate of drug release decreased. Formulation F27 sustained release up to 24 h. The reason for this can be attributed to the formation of a stronger gel layer around the tablet, acting as a barrier for the release of drug. Formulation F27 was selected as the best formulation keeping in view the amount required for sustaining the release up to a period of 24 h.

DISCUSSION

The Metformin Hcl solution was scanned in UV for determination of λmax. UV spectrum of Metformin Hcl was found to be at 234 nm in phosphate buffer pH 6.8 and also the same wavelength was observed in 0.1N Hcl(pH 1.2).

Fourier Transformed Infrared (FT-IR) Spectroscopic Interaction: FT-IR spectra of pure drug (metformin HCl) showed characteristic bands at 3371.64 $cm^{-1,}$ 3167.12 cm^{-1} and 1628.13 cm^{-1} assigned to primary, secondary N-H stretching and N-H deformation respectively. There were three absorption peaks at 936.48 cm^{-1}, 1444.61 cm^{-1}, 1417.68 cm^{-1} assigned to CH_3 rocking, CH_3 asymmetric and CH_3 symmetric deformation respectively. The peaks observed at 1062.78 cm^{-1} was assigned to C-N stretching. The peaks observed at 1566.20 cm^{-1} was assigned to NCN asymmetric stretching. The above peaks were also observed for the granules prepared using different polymers like HPMC 100 cps, xanthan gum and *Lannea*

coromandelica gum. Hence there is no interaction between metformin HCl and polymers used in the present research work (Figure 3-6 and table 3).

Differential scanning calorimetry (DSC) study: A DSC study was performed for metformin HCl and granules containing xanthan gum, HPMC 100 cps and *Lannea coromandelica* gum. DSC thermogram of metformin HCl showed an endothermic peak at 231.2^0C with onset and end set temperatures of 228.3^0C and 236.5^0C respectively. The latent heat of fusion *(ΔH_{fus})* was found to be -2.71 J indicating crystalline nature of the drug [24, 25, 26]. Similarly DSC study was also performed for the granules prepared with different polymers. DSC thermogram of HPMC 100 cps based granules showed endothermic peak at 228.17^0C with onset and end set temperatures of 221.52^0C and 235.4^0C respectively. The granules also exhibited negative values of latent heat of fusion *(ΔH_{fus})* i.e. -2.05 J. DSC thermogram of xanthan gum based granules showed endothermic peak at 222.75^0C with onset and end set temperatures of 219.63^0C and 228.44^0C respectively. The granules also exhibited negative values of latent heat of fusion *(ΔH_{fus})* i.e. -1.43 J. DSC thermogram of *Lannea coromandelica* gum based granules showed endothermic peak at 209.68^0C with onset and end set temperatures of 204.05^0C and 228.18^0C respectively. The granules also exhibited negative values of latent heat of fusion *(ΔH_{fus})* i.e. -1.03 J. The DSC study exhibited that granules have shown endothermic peaks nearly similar to that of the pure drug with negative latent heat of fusion. Hence there is no interaction between metformin Hcl and polymers used in the present research. Granules of metformin Hcl were prepared using three different polymers namely Xanthan gum, HPMC 100 cps and *Lannea coromandelica* gum. All the three polymers showed good swelling and binding property upon contact with water. The granules were prepared using distilled water as a granulating fluid without using any other binder solution. Hence this approach can be considered as an economic approach for the preparation of tablets by wet granulation method. The values of angle of repose (36°), C.I (26 %) and H.R (1.36) for pure drug (metformin Hcl) suggest that the flowability and compressibility were not within the theoretical range for processing into tablet dosage form. But granules prepared by using different polymers showed significant improvement in flowability due to increase in particle size (granules), density, spherical nature of granules and lubrication effect of talc and magnesium stearate s glidant (Table 4). One of the most important factors affecting bulk density of a powder and its flow properties is the interparticulate friction [17]. Desirable micromeritics properties can increased bulk density for granules revealed enhanced flowability [18]. Similarly, increased tapped density for granules indicated better degree of compactibility as a function of applied pressure [19]. Granular friability index indicate good bonding properties of the prepared granules. It revealed that addition of water to the dry mix of drug and polymer increased the binding between the particles. The loss of powder from surface of granules during friability testing was less than 1 % suggesting all the three polymers imparted optimum binding to granules (Table 4). Lower value of '*a*' for all the three polymer based granules revealed better flowability than pure drug metformin Hcl. Whereas, lower value of '*1/b*' for all granules showed that it was less cohesive than pure drug metformin HCl which may be because of dense particles (Table 5). Generally dense particles are less cohesive to enhance flowability [20]. Standard calibration curve was plotted between absorbance Vs concentration of metformin Hcl. A good linear relationship was observed with correlation coefficient (r^2) of 0.999. Beer's law range was found in

the range of 5-600 µg/ml(Table 6 and Fig 7).

***In- vitro* dissolution study from prepared granules**

In-vitro dissolution study for the xanthan gum based metformin Hcl granules showed that as the concentration of xanthan gum increased the release rate decreased. The effect of xanthan gum concentration, on the release of water soluble drug metformin HCl was studied. The granules were formulated in the following drug-polymer ratios i.e. 1: 0.1, 1:0.2, 1: 0.4, 1:0.6, 1:0.8 and 1:1 designated as formulation F1, F2, F3, F4, F5 and F6 respectively (Fig 8). The release rate was found to be decreasing as the concentration of polymer increased. Formulation F1 and F2 could not sustain the release of drug beyond 6 h whereas formulation F3 could sustain the release only up to 8 h. Formulations F1, F2 and F3 underwent erosion before complete swelling could take place, resulting in drug release initially and then sustained the drug release up to 6 and 8 h respectively. Formulation F4, F5 and F6 were able to sustain the release up to 10 h. None of the xanthan gum based granules of metformin HCl could sustain the release up to 24 h. But as formulations F4, F5, and F6 have shown some promising sustaining property, these formulations were selected for compression into matrix tablets.

Similarly *In-vitro* dissolution study for the HPMC 100 cps based metformin HCl granules showed that as the concentration of HPMC 100 cps increased the release rate decreased. The effect of HPMC 100 cps concentration, on the release of water soluble drug metformin HCl was studied. The granules were formulated in the following drug - polymer ratios i.e. 1: 0.1, 1:0.2, 1: 0.4, 1:0.6, 1:0.8 and 1:1 designated as formulation F7, F8, F9, F10, F11 and F12 respectively (Fig 9). The release rate was found to be decreasing as the concentration of HPMC 100 cps increased. Formulation F7, F8 and F9 could not sustain the release of drug beyond 6 h whereas formulation F10 could sustain the release only up to 8 h. Formulation F11 and F12 were able to sustain the release up to 12 h. None of the HPMC 100 cps based granules of metformin Hcll could sustain the release up to 24 h. But as formulations F10, F11, and F12 have shown some promising sustaining property, these formulations were selected for preparation of matrix tablets. *In-vitro* dissolution study for the *Lannea coromandelica* gum based metformin HCl granules showed that as the concentration of *Lannea coromandelica* gum increased the release rate decreased. The effect of *Lannea coromandelica* gum concentration, on the release of water soluble drug metformin HCl was studied. The granules were formulated in the following drug to polymer ratios i.e. 1: 0.1, 1:0.2, 1: 0.4, 1:0.6, 1:0.8 and 1:1 designated as formulation F13, F14, F15, F16, F17 and F18 respectively (Fig 10). The release rate was found to be decreasing as the concentration of *Lannea coromandelica* gum increased. Formulation F13, F14, F15 and F16 could not sustain the release of drug beyond 6 h. whereas F17 and F18 were able to sustain the release up to 12 h. None of the *Lannea coromandelica* gum based granules of metformin HCl could sustain the release up to 24 h. But as formulations F16, F17, and F18 have shown some sustaining property, these formulations were selected for preparation of matrix tablets.

Release characteristics of Metformin Hcl matrix tablets prepared employing various polymers: The release profiles are given in Fig 11- Fig 13. Drug release parameters are summarized in Table.7. Metformin Hcl release from all the matrix tablets was slow and spread over a period of 24 h of long period of time. It was depended on polymer ratio. Release data were analysed as per zero order, first order, Higuchi[21], Peppas[20, 22] equation models to assess the drug release kinetics and mechanism from the matrix tablets.

The correlation coefficient (r^2) values in the analysis of release data as per different kinetic models are given in Table.7. The analysis of release data as per zero and first order kinetics models indicated that metformin Hcl release from all the xanthn gum, HPMC 100 cps and *lannea coromandelica* gum followed first order kinetics. Correlation coefficient (r^2) values were higher in the first order model than those in the zero order model with these matrix tablets indicating that the drug release from these matrix tablets followed first order kinetics (Table.7). To evaluate the drug release mechanism from the matrix tablets prepared, plots of percent released verses square root of time were constructed. These plots were found to be linear with all the polymer matrix tablets with correlation coefficient (r^2) values > 0.956. These plots indicated that the drug release mechanism from the matrix tablets prepared employing various polymers were diffusion controlled. When the release pattern data were analysed as per the Peppas equation, the release exponent (n) was in the range of 0.241-0.444 in the all matrix tablets indicating that the release mechanism from these matrix tablets were by Fickian diffusion. The results of the study indicated that the metformin Hcl release from the matrix tablets prepared employing all the three polymers namely (i) xanthn gum (ii) HPMC 100 cps (iii) *lannea coromandelica* gum (new polymer) was slow and spread over a 24 h and from the three polymers matrix tablets were found suitable for controlled release. Matrix tablets of metformin Hcl were prepared employing Xanthan gum, HPMC 100 cps and *Lannea coromandelica* gum in different strengths in the tablets by wet granulation method. Xanthan gum, HPMC 100 cps and *Lannea coromandelica* gum were used at 0.6, 0.8 and 1.0 % strengths in the matrix tablets. Metformin Hcl release profiles of the matrix tablets prepared employing Xanthan gum, HPMC 100 cps and *Lannea coromandelica* gum were given in Fig.11- Fig 13. Metformin Hcl from the matrix tablets prepared rate release was slow and spread over 24 h and depended on the strength (%) of Xanthan gum, HPMC 100 cps and *Lannea coromandelica* gum in the matrix tablets. As strength of Xanthan gum, HPMC 100 cps and *Lannea coromandelica* gum in the matrix tablets was increased drug release was decreased. As the proportion of polymer ratio increased, metformin Hcl release rate was decreased. Good linear relationships were observed between (i) polymer concentration and release rate constant (k_1) values. The relationships could be expressed by the following linear equations.

$Y = -0.378 X+0.509$

Where Y is release rate constant (K_1, h^{-1}) and X is polymer concentration

$Y = -0.172 X +0.323$

Where Y is release rate constant (K_1, h^{-1}) and X is polymer concentration

$Y = -0.247 X +0.384$

Where Y is release rate constant (K_1, h^{-1}) and X is polymer concentration. The release rate (K_1) was decreased as the strength of HPMC 100 cps, Xanthan gum and *Lannea coromandelica* gum in the matrix tablets was increased. Hence, drug release from the matrix tablets could be controlled by varying the strength (%) of Xanthan gum, HPMC 100 cps and *Lannea coromandelica* gum in the matrix tablets. The results of the study, thus, indicated that Xanthan gum, HPMC 100 cps and *Lannea coromandelica* gum could be used as release retardant and rate controlling matrix former in the design of matrix tablets for controlled release of metformin Hcl. But the metformin Hcl release from the Xanthan gum, HPMC 100 cps and *Lannea coromandelica* gum matrix tablets was very slow and low even at a very low concentration of 1 % in the formula. At 1% concentration of Xanthan gum, HPMC 100 cps and *Lannea coromandelica* gum in the matrix tablets the release was 98.48±0.17, 99.91±0.41 and 96.67±1.11% in 24 h.

Table 1: Composition of Metformin HCl granules prepared by using Xanthan gum, HPMC 100 cps and *Lannea coromandelica* gum

Code	Ingredients (mg)							
	Metformin Hcl	Xanthan gum	HPMC 100 cps	Lannea coromandelica gum	Lactose	Talc	Mg. stearate	Total weight (mg)
F1	500	50	-	-	450	10	10	1020
F2	500	100	-	-	400	10	10	1020
F3	500	200	-	-	300	10	10	1020
F4	500	300	-	-	200	10	10	1020
F5	500	400	-	-	100	10	10	1020
F6	500	500	-	-	0	10	10	1020
F7	500	-	50	-	450	10	10	1020
F8	500	-	100	-	400	10	10	1020
F9	500	-	200	-	300	10	10	1020
F10	500	-	300	-	200	10	10	1020
F11	500	-	400	-	100	10	10	1020
F12	500	-	500	-	0	10	10	1020
F13	500	-	-	50	450	10	10	1020
F14	500	-	-	100	400	10	10	1020
F15	500	-	-	200	300	10	10	1020
F16	500	-	-	300	200	10	10	1020
F17	500	-	-	400	100	10	10	1020
F18	500		-	500	0	10	10	1020

Table 2: Composition of metformin HCl matrix tablets prepared by using Xanthan gum, HPMC 100 cps and *Lannea coromandelica* gum

Ingredients (mg)	F19	F20	F21	F22	F23	F24	F25	F26	F27
Metformin HCl	500	500	500	500	500	500	500	500	500
Xanthan gum	300	400	500	-	-	-	-	-	-
HPMC 100 cps	-	-	-	300	400	500	-	-	-
Lannea coromandelica gum	-	-	-	-	-	-	300	400	500
Lactose	200	100	0	200	100	0	200	100	0
Talc	10	10	10	10	10	10	10	10	10
Magnesium stearate	10	10	10	10	10	10	10	10	10
Total weight	1020	1020	1020	1020	1020	1020	1020	1020	1020

Table 3: Functional groups in FT-IR spectra of metformin HCl and polymers

Assignment of bands	Metformin HCl	Drug + HPMC 100 cps	Drug+ Xanthan Gum	Drug + Lannea coromandelica gum
N-H stretch (1° Amine)	3371.64	3369.64	3369.64	3369.64
N-H deformation	1628.13	1625.99	1624.06	1625.99
N-H stretch (2° Amine)	3167.12	3161.33	3165.19	3157.47
C-N stretch	1062.78	1064.71	1064.71	1064.71
CH_3 rock	936.48	937.40	937.40	937.40
CH_3 asymmetric	1446.61	1473.62	1473.62	1473.62
CH_3 symmetric deformation	1417.68	1419.61	1419.61	1419.61
NCN asymmetric	1566.20	1568.13	1568.13	1558.48

stretch				

Table 4: Data of micromeretics properties of metformin HCl and its prepared granules

Code	Angle of repose (^{0})*	Compressibility index (%) *	Hausner's ratio*	Granular friability index	Compactibility(a)*	Cohesiveness (1/b)*	Regression coefficient (r^2)
Metformin	**36.12±1.2**	**26.01±0.9**	**1.34±0.2**	**-**	**0.382 ± 0.01**	**13.77 ± 0.03**	**0.998**
F19	**25.98±0.4**	**15.02±0.2**	**1.25±0.1**	**0.125**	**0.181 ± 0.03**	**8.42 ± 0.02**	**0.996**
F20	**25.08±1.1**	**16.04±0.7**	**1.24±0.2**	**0.652**	**0.185 ± 0.02**	**8.45 ± 0.05**	**0.997**
F21	**24.09±1.2**	**16.99±0.5**	**1.22±0.4**	**0.385**	**0.190 ± 0.04**	**8.56 ± 0.10**	**0.997**
F22	**22.12±1.1**	**20.05±0.5**	**1.22±0.3**	**0.472**	**0.173 ±0.05**	**11.35±0.29**	**0.995**
F23	**24.09±1.0**	**15.11±0.6**	**1.21±0.2**	**0.152**	**0.141±0.06**	**11.79±0.42**	**0.996**
F24	**23.13±1.2**	**19.11±0.4**	**1.21±0.4**	**0.541**	**0.135 ±0.08**	**11.45±0.19**	**0.997**
F25	**24.11±1.1**	**18.11±0.4**	**1.25±0.5**	**0.591**	**0.214±0.09**	**10.16±1.26**	**0.998**
F26	**24.10±0.9**	**17.01±0.6**	**1.23±0.1**	**0.185**	**0.194±0.11**	**9.82±1.32**	**0.995**
F27	**23.11±0.5**	**18.11±0.5**	**1.23±0.4**	**0.590**	**0.211±0.15**	**10.16±1.35**	**0.996**

***All values are expressed as Mean ± S.D, *n* = 6, - Not applicable**

Table 5: Quality control tests for prepared matrix tablets of metformin HCl

Formulation	Hardness (Kg/Cm^2) *	Friability (%)*	Weight variation*	Drug content (%)*
F19	**5.12±0.58**	**0.41±0.71**	**0.721±0.08**	**95.81±0.67**
F20	**4.91±0.98**	**0.44±0.48**	**0.313±0.02**	**97.90±0.99**
F21	**4.60±0.29**	**0.39±0.09**	**0.214±0.07**	**98.41±0.27**
F22	**5.10±0.87**	**0.35±0.07**	**0.823±0.03**	**96.90±0.61**
F23	**4.91±0.48**	**0.37±0.06**	**0.911±0.81**	**97.21±0.87**
F24	**5.10±0.14**	**0.42±0.10**	**0.782±0.07**	**96.51±0.14**
F25	**5.31±0.24**	**0.32±0.02**	**0.634±0.15**	**94.91±0.51**
F26	**5.21±0.21**	**0.54±0.07**	**0.910±0.11**	**98.22±0.47**
F27	**5.61 ±0.23**	**0.24±0.05**	**0.992±0.12**	**97.53±0.36**

***Mean ± SD, n = 6**

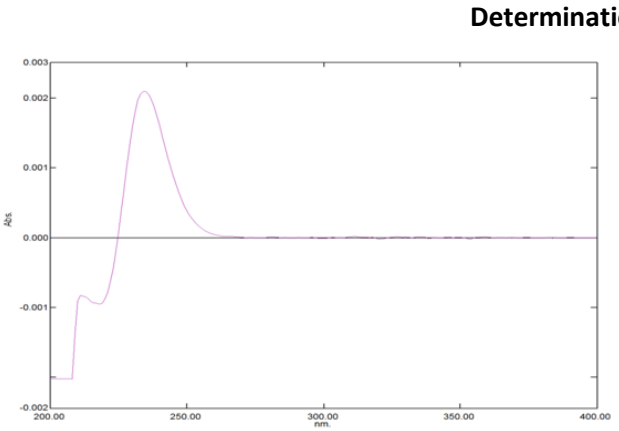

Fig1: UV scanning of metformin HCl in SGF (pH 1.2)

Determination λ max

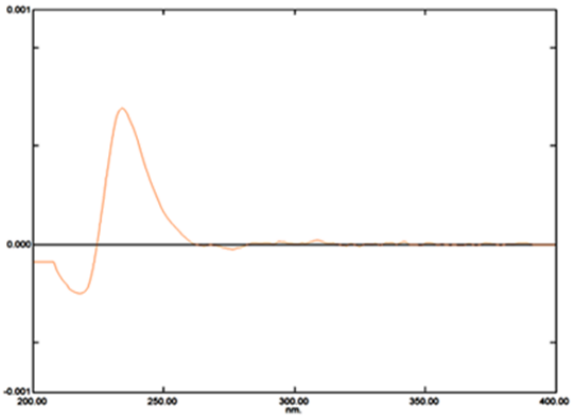

Fig 2: UV-spectrum of metformin Hcl in SIF without enzyme

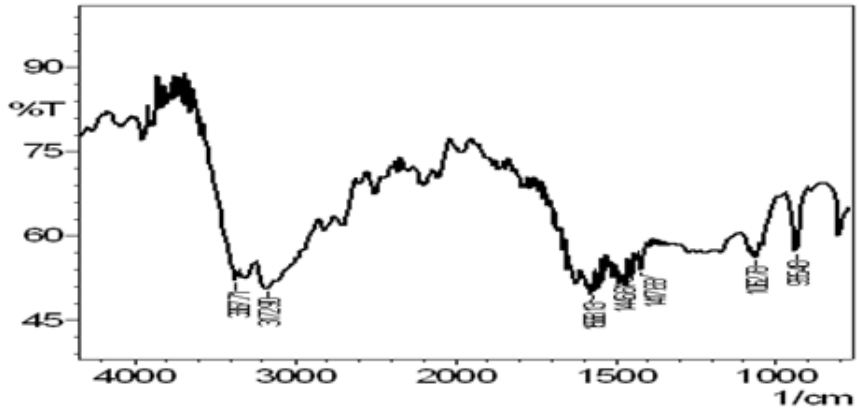

Fig 3: FT-IR spectra of metformin HCl

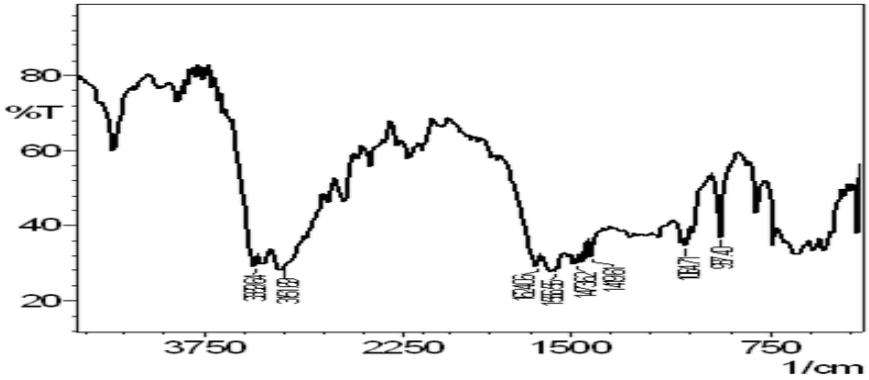

Fig 4: FT-IR spectra of metformin HCl – Xanthan gum

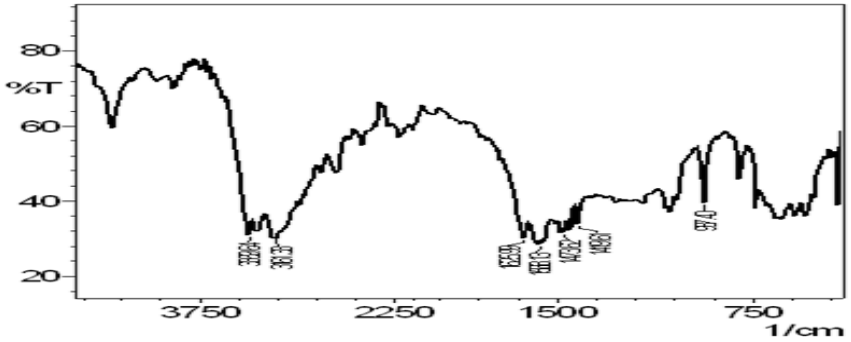

Fig 5: FTIR spectra of metformin HCl – HPMC 100 cps

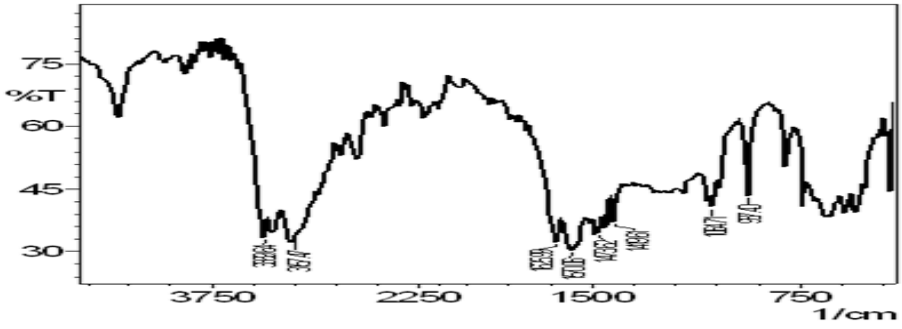

Fig 6: FT-IR spectra of metformin HCl - *Lannea coromandelica* gum

Table 6: Standard plot of metformin Hcl in SIF without enzyme

S.No	Concentration (µg/ml)	Absorbance	RSD (%)
1	5	0.106	0.110
2	10	0.221	0.123
3	15	0.328	0.134
4	20	0.435	0.286
5	25	0.542	0.346
6	30	0.651	0.412
7	40	0.881	0.314
8	50	1.097	0.367
9	60	1.320	0.218

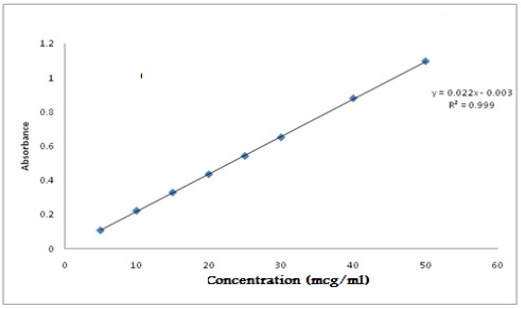

Fig 7: Standard plot of metformin Hcl in SIF without enzyme at 234 nm

Table 7: Release kinetics and Drug release parameters of matrix tablets of metformin

Code	Correlation coefficient (r^2)				Peppas release exponent (n)	Drug release parameters			
	Zero order	First order	Higuchi	Peppas		T_{50} (h)	T_{90} (h)	K_0 (mg/ h)	K_1 (h^{-1})
F19	0.613	0.984	0.853	0.962	0.241	1.3	8.4	3.052	0.301
F20	0.678	0.965	0.897	0.980	0.271	1.4	8.7	3.215	0.285
F21	0.898	0.925	0.992	0.980	0.437	6.0	17.7	3.664	0.147
F22	0.621	0.963	0.861	0.956	0.262	1.2	8.4	3.120	0.246
F23	0.737	0.948	0.930	0.976	0.262	2.0	8.4	3.448	0.280
F24	0.795	0.957	0.955	0.973	0.383	3.7	11.5	0.122	0.278
F25	0.664	0.973	0.888	0.977	0.265	1.2	10/3	3.176	0.290
F26	0.795	0.948	0.956	0.977	0.376	3.8	12.2	3.678	0.237
F27	0.903	0.960	0.996	0.993	0.444	6.2	19.1	3.598	0.124

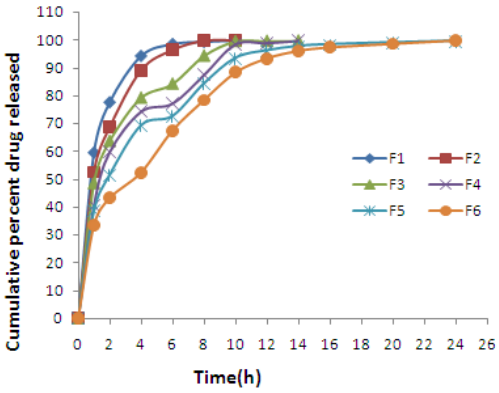

Fig 8: Dissolution profile of metformin Hcl from xanthan gum CR matrix granules

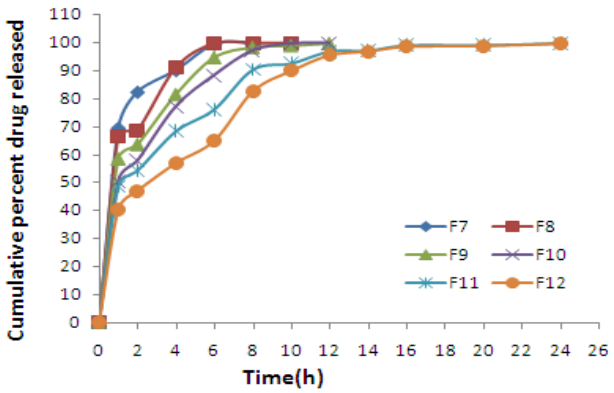

Fig 9: Dissolution profile of metformin Hcl from HPMC 100 cps CR matrix granules

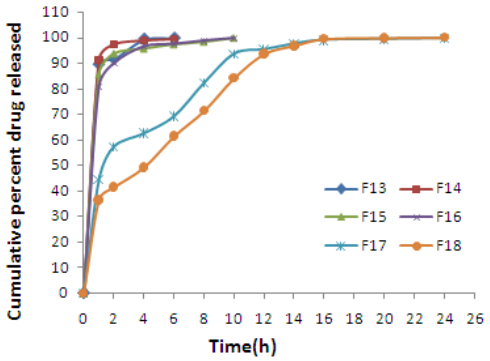

Fig 10 : Dissolution profile of metformin Hcl *from Lannea coromandelica* gum based CR matrix granules

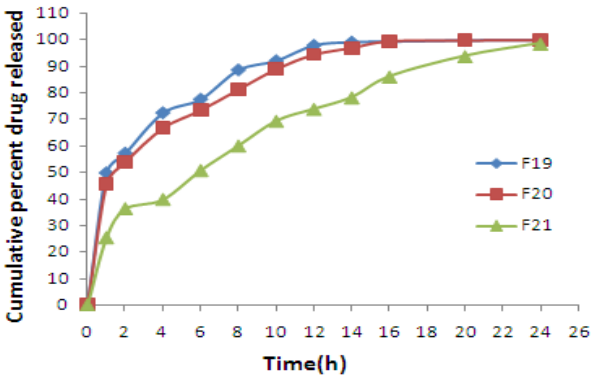

Fig 11 : Dissolution profile of CR matrix tablets of metformin HCl employed xanthan gum

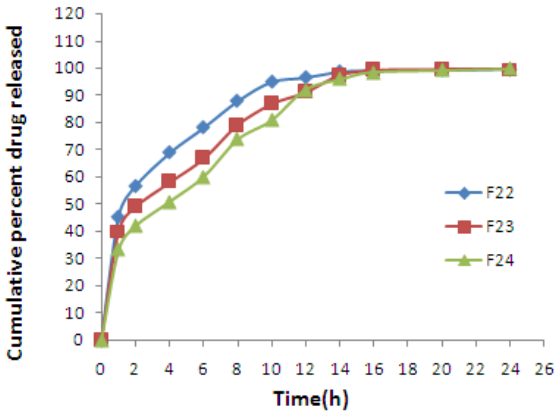

Fig 12: Dissolution profile of CR matrix tablets of metformin HCl employed HPMC 100 cps

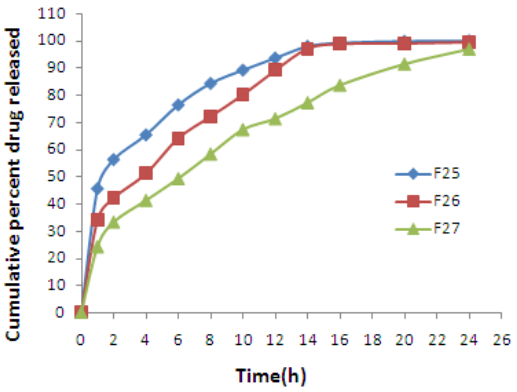

Fig 13: Dissolution profile of CR matrix tablets of metformin HCl employed *Lannea coromandelica* gum

These matrix tablets formulations prepared fulfilled the official (USP 30) release specification prescribed for metformin Hcl extended release tablets. Finally we conclude that the controlled release matrix tablets of metformin HCl, a BCS class III drug can be prepared by wet granulation method employing a novel polymer *Lannea coromandelica* gum. This gum showed similar sustaining and swelling properties compared to established polymers like HPMC 100 cps and xanthan gum. Hence this gum has the potential to sustain and retarding the release of a highly water soluble drug like metformin HCl. Hence *Lannea coromandelica* gum needs to explore as a controlled release material at commercial scale.

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