Research in Pharmaceutical Sciences, February 2012; 7(1): 57-64
Received: May 2011
Accepted: Sep 2011

School of Pharmacy & Pharmaceutical Sciences
Isfahan University of Medical Sciences

***Original Article***

# Preparation and *in vitro* evaluation of guar gum based triple-layer matrix tablet of diclofenac sodium

**H.V. Chavda*, M.S. Patel and C.N. Patel**

*Shri Sarvajanik Pharmacy College, Gujarat Technological University, Nr. Arvind Baug, Mehsana, Gujarat, India.*

## *Abstract*

The objective of the present study was to design an oral controlled drug delivery system for sparingly soluble diclofenac sodium (DCL) using guar gum as triple-layer matrix tablets. Matrix tablet granules containing 30% (D1), 40% (D2) or 50% (D3) of guar gum were prepared by the conventional wet granulation technique. Matrix tablets of diclofenac sodium were prepared by compressing three layers one by one. Centre layer of sandwich like structure was incorporated with matrix granules containing DCL which was covered on either side by guar gum granule layers containing either 70, 80 or 87% of guar gum as release retardant layers. The tablets were evaluated for hardness, thickness, drug content, and drug release studies. To ascertain the kinetics of drug release, the dissolution profiles were fitted to various mathematical models. The *in vitro* drug release from proposed system was best explained by the Hopfenberg model indicating that the release of drug from tablets displayed heterogeneous erosion. D3G3, containing 87% of guar gum in guar gum layers and 50% of guar gum in DCL matrix granule layer was found to provide the release rate for prolonged period of time. The results clearly indicate that guar gum could be a potential hydrophilic carrier in the development of oral controlled drug delivery systems.

***Keywords:*** Triple-layer matrix tablet; Guar gum; Diclofenac sodium

## INTRODUCTION

A natural non-ionic polysaccharide, Guar gum, is derived from the seeds of *Cyamopsis tetragonolobus* (Family Leguminosae). Pharmaceutically, guar gum is used as a binder and/or disintegrant in solid dosage forms, and as a suspending, thickening and stabilizing agent in liquid oral and topical products. Therapeutically, it is used as a part of the diet of the diabetic patients. On exposure to dissolution fluids guar gum gets hydrated and forms a viscous gel layer that retards further seeping-in of dissolution fluids towards the core of the matrix tablets (1-4).

The viscous gel layer strength around the core of the matrix tablets depends on particle size, compression force, other excipients presence, polymer viscosity, drug solubility and others. The presence of Hydroxy propyl methyl cellulose (HPMC) also plays an important role in matrix tablets. The HPMC hydrates on exposure to aqueous fluids to form a viscous gel layer and due to the erosion of the matrix and/or the diffusion process, the drug gets released (5).

Diclofenac sodium (DCL) is the most commonly used NSAIDs, useful in the treatment of rheumatic disorders. It is characterized by rapid systemic clearance, and so used in sustain release (SR) formulations for prolonged action to improve patient compliance (6,7). Therefore, DCL is a good candidate for SR formulation (8,9).

Multiple layers of release retardant polymer are applied on both sides of a matrix tablet such that the hydrophilic polymer swells and controls the drug release after oral administration. These formulations deliver the drug at a controlled, predetermined rate and maintain systemic therapeutically effective concentrations for prolonged time period. The widely used polymers for sustaining the drug delivery are cellulose derivatives, chitosan, eudragits, and natural gums (10). Layered tablet concept has been applied for

*Corresponding author: Chavda Hitesh V.
Email: hvchavda@sspcmsn.org

trimetazidine dihydrochloride (10), diltiazem hydrochloride (11), metoprolol tartrate (12), venlafaxine hydrochloride (13,14), and others.

The present study describes the development and evaluation of oral controlled drug delivery systems for sparingly water soluble DCL using guar gum as a carrier in the form of triple-layer matrix tablets.

## MATERIALS AND METHODS

### *Materials*

DCL was a generous gift from Torrent Pharmaceutical Ltd, Ahmedabad, India. The pharmaceutical grade guar gum was a generous gift from H. B. Gum Industries Pvt. Ltd, Kalol, India. HPMC, starch, magnesium stearate, talc, and solvents were purchased from SD Fine Chem. Ltd, Mumbai, India. Double distilled water (DDW) and phosphate buffer pH 6.8 were prepared in laboratory. All other chemicals used were of analytical grade and used as obtained.

### *Preparation of DCL matrix granules*

The wet granulation technique was used for the preparation of matrix granules of DCL. DCL matrix granule formulations were prepared with 30% (D1), 40% (D2), and 50% (D3) of guar gum. The guar gum, DCL, and HPMC were blended using 10% starch paste as a binder. The wet mass was passed through a mesh (10#) and the granules were dried for 2 h at 50°C. The dried granules were passed through mesh (20#) and were lubricated with talc and magnesium stearate. The composition of DCL matrix granule formulations containing 50 mg of DCL is shown in Table 1.

### *Preparation of guar gum granules*

The wet granulation technique was used for the preparation of guar gum granules. The granules were prepared with 70, 80, or 87% of guar gum and were coded as Gl, G2, and G3, respectively. The guar gum and HPMC were blended and granulated with 10% starch paste. The wet mass was passed through a mesh (10#) and the granules were dried for 2 h at 50°C. The dried granules were passed through a mesh (20#) and were lubricated with talc and magnesium stearate. The composition of guar gum granules is shown in Table 2.

### *Preparation of triple-layer matrix tablets*

DCL triple-layer matrix tablets were prepared by compressing (11 mm diameter, flat punch) 200 mg of guar gum granules containing either 70% (G1), 80% (G2), or 87%

**Table 1.** Composition of DCL matrix tablet granules

| Ingredients | Quantity (mg) | | |
|---|---|---|---|
| | D1 | D2 | D3 |
| DCL | 50 | 50 | 50 |
| Guar gum | 60 | 80 | 100 |
| Starch | 20 | 20 | 20 |
| HPMC | 64 | 44 | 24 |
| Talc | 04 | 04 | 04 |
| Magnesium stearate | 02 | 02 | 02 |
| Total weight (mg) | 200 | 200 | 200 |

**Table 2.** Composition of guar gum granules

| Ingredients | Quantity (mg) | | |
|---|---|---|---|
| | G1 | G2 | G3 |
| Guar gum | 140 | 160 | 174 |
| Starch as paste | 20 | 20 | 20 |
| HPMC | 34 | 14 | 0 |
| Talc | 4 | 4 | 4 |
| Magnesium stearate | 2 | 2 | 2 |
| Total weight (mg) | 200 | 200 | 200 |

(G3) of guar gum on either sides of DCL matrix granules containing either 30% (D1), 40% (D2) or 50% (D3) of guar gum. The respective batches were coded as G1D1, G1D2, G2D1, G2D2, G2D3, G3D1, G3D2, and G3D3. For the preparation of tablets first DCL-matrix granules containing were prepared by wet granulation method for the matrix formulation. Then guar gum granules for layering over the DCL matrix granules were prepared. The volume of the die cavity was adjusted to 600 mg. Bottom layer was prepared by slight compression of guar gum granules, 200 mg, in the die cavity, which provided uniform spreading. The upper punch was lifted up, and DCL matrix granules (for middle layer), 200 mg, were placed over the prepared bottom layer in the die cavity and slightly compressed once again. Finally, 200 mg of guar gum granules (for top layer) were placed over the middle layer and compressed (Rimek, India) with a maximum compression force. Schematic diagram for triple-layer matrix tablet is shown in Fig. 1.

### *Evaluation of tablets*

The preparedtriple-layer matrix tablets were evaluated for their hardness, thickness, weight variation, friability and drug content. The hardness (n=5), friability (n=10) and thickness (n=5) oftriple-layer matrix tablets were determined using the Pfizer type hardness tester (Janki Impex, Ahmedabad), the Roche friabilator (Electrolab, India), and the thickness gauge (Mitutoyo, Japan), respectively.

The weight variation test was performed according to Indian Pharmacopoeia 2007. For estimation of drug content, 10 tablets were crushed, and the aliquots of powder equivalent to 100 mg of drug were extracted in phosphate buffer pH 6.8. The solutions were passed through 0.45 µm membrane filter and after suitable dilutions the absorbance was measured at 276 nm using the UV-1800 UV/VIS Double Beam Spectrophotometer (Shimadzu, Japan).

### *In Vitro dissolution studies*

The release rate of DCL from triple-layer matrix tablets ($n$=3) was determined using USP XXIV dissolution testing apparatus II (dissolution tester model TDT-08 L, Electrolab, India). The dissolution test was performed using 900 ml phosphate buffer pH 6.8 at 37 ± 0.5°C and 75 rpm. The aliquots (5 ml) were withdrawn from the dissolution tester hourly for 12 h, and replaced with fresh dissolution medium, immediately. The samples were passed through 0.45 µm membrane filter and diluted (if needed) to a suitable concentration

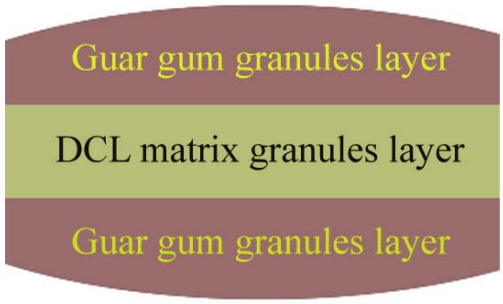



**Fig. 1.** Schematic diagram oftriple-layer matrix tablet of DCL

**Table 3.** Mathematical Models used to ascertain drug release (15,16)

| Mathematical Model | Equation |
|---|---|
| Zero-order | $Q_t = Q_0 + K_0 t$ |
| First-order | $ln\ Q_t = ln\ Q_0 + K_1 t$ |
| Higuchi | $Q_t = K_H t^{1/2}$ |
| Hixson-Crowell | $Q_0^{1/3} - Q_t^{1/3} = K_s t$ |
| Korsmeyer-Peppas | $Q_t/Q_\infty = K_k t^n$ |
| Weibull | $\log [-\ln (1 - m)] = \beta \log (t - T_i) - \log \alpha$ |
| Hopfenberg | $Q_t/Q_\infty = 1 - [1 - k_0 t/C_0 a_0]^{n2}$ |

$Q_t$: amount of drug released in time $t$, $Q_0$: initial amount of drug in the dosage form, $Q_\infty$: total amount of drug dissolved when the dosage form is exhausted, $K_0$, $K_1$, $K_H$, $K_s$, $K_k$, $k_0$: release rate constants, $n$: release exponent (indicative of drug release mechanism), $m$: accumulated fraction of the drug, $\beta$: shape parameter, $\alpha$: scale parameter, $T_i$: location parameter, $C_0$ : initial concentration of drug in the dosage form, $a_0$: initial radius for a sphere or cylinder or the half-thickness for a slab, $n2$: 1, 2 and 3 for a slab, cylinder and sphere, respectively.

with dissolution medium. The absorbance of solutions was measured at 276 nm using UV-1800 UV/VIS Double Beam Spectrophotometer (Shimadzu, Japan). The cumulative percentage of drug release was calculated using an equation obtained from the standard curve.

### *Kinetics of drug release*

The *in vitro* drug release data were analyzed by fitting them to different kinetic models (15,16) as shown in Table 3 in order to study the release kinetics and mechanism of drug fromtriple-layer matrix tablets.

### *Stability studies*

The optimized batch was kept in airtight containers and stored in the stability chamber (TH-90S, Thermolab, India) at 40°C/75% relative humidity (RH) for six months (17). Results for *in vitro* dissolution studies obtained after and before six months were compared. The similarity factor ($f_2$) was applied to study the effect of storage on optimized batch. The $f_2$ value (18) is calculated from this equation:

$$f_2 = 50 \text{ x } \log \{[1 + (1/n) \sum_{j=1}^{n} |R_j - T_j|^2]^{-0.5} \text{ x } 100\}$$

where, $n$ is the number of dissolution time points and $R_j$ and $T_j$ are the percent dissolved of the reference product and test product at each time point $j$, respectively.

## RESULTS

### *Evaluation of tablets*

The evaluation parameters for DCLtriple-layer matrix tablets are shown in Table 4.

### *In Vitro dissolution studies*

All tablets were found swollen till the end of 12 h dissolution study. The swollen tablets edges were slightly eroded. Fig. 2 shows the dissolution profile of DCL triple-layer matrix tablets in phosphate buffer pH 6.8.

**Table 4.** Evaluation parameters for DCL matrix tablets

| Batch | Thickness[a] (mm) | Hardness[a] (kg/cm$^2$) | Friability[b] (%) | Deviation in weight variation test[c] (%) | Drug content[b] (%) |
|---|---|---|---|---|---|
| D1G1 | 3.51 ± 0.05 | 6.8 ± 0.12 | 0.41 ± 0.06 | 3.37 ± 0.05 | 98.49 ± 0.08 |
| D1G2 | 3.56 ± 0.04 | 6.8 ± 0.15 | 0.36 ± 0.03 | 3.53 ± 0.08 | 98.37 ± 0.05 |
| D1G3 | 3.58 ± 0.04 | 6.9 ± 0.09 | 0.34 ± 0.06 | 2.99 ± 0.05 | 98.69 ± 0.06 |
| D2G1 | 3.54 ± 0.04 | 6.7 ± 0.16 | 0.49 ± 0.07 | 3.32 ± 0.07 | 98.32 ± 0.05 |
| D2G2 | 3.53 ± 0.05 | 6.7 ± 0.13 | 0.39 ± 0.03 | 3.23 ± 0.05 | 98.37 ± 0.04 |
| D2G3 | 3.52 ± 0.06 | 6.5 ± 0.11 | 0.45 ± 0.08 | 3.71 ± 0.03 | 98.52 ± 0.06 |
| D3G1 | 3.56 ± 0.05 | 6.9 ± 0.05 | 0.29 ± 0.06 | 3.64 ± 0.09 | 98.23 ± 0.04 |
| D3G2 | 3.53 ± 0.03 | 6.8 ± 0.08 | 0.48 ± 0.06 | 3.26 ± 0.07 | 99.68 ± 0.08 |
| D3G3 | 3.57 ± 0.04 | 6.8 ± 0.14 | 0.37 ± 0.08 | 3.62 ± 0.05 | 98.32 ± 0.06 |

[a]Mean ± SD, n=5, [b] Mean ± SD, n=10, [c] Mean ± SD, n=20

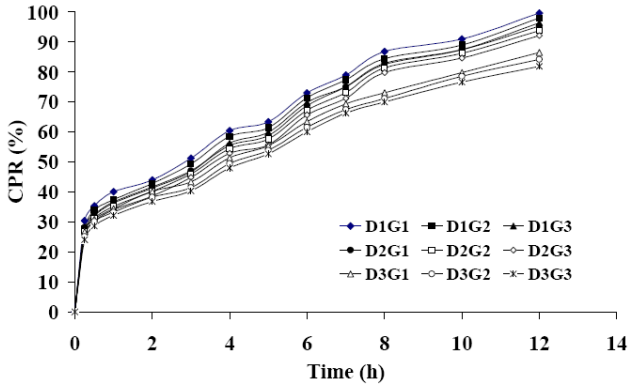
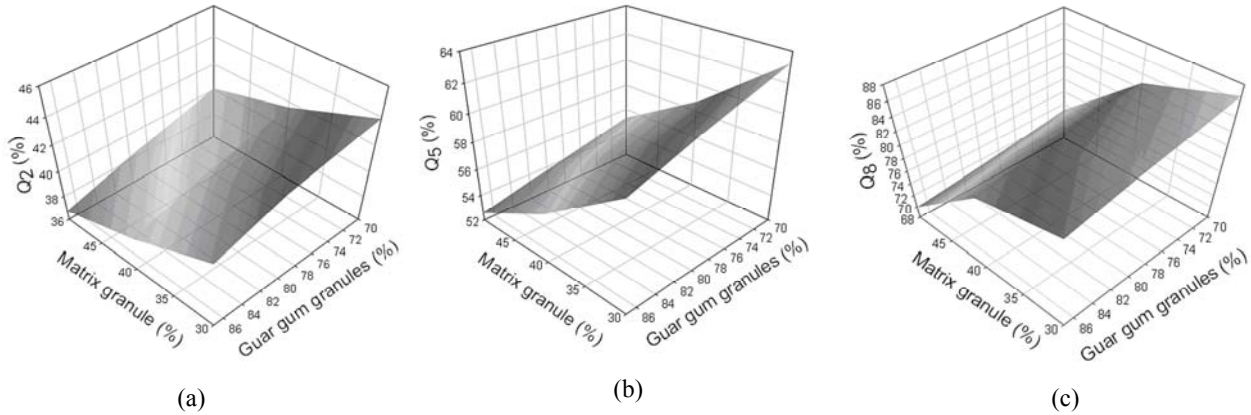



**Fig. 2.** *In vitro* dissolution profile of DCL from tablets in Phosphate buffer pH 6.8 (Mean, n=3, CPR stands for cumulative percent released)




(a) (b) (c)

**Fig. 3.** Response surface plots showing the effect of guar gum granules and matrix granules proportions on the drug release at (a) 2 h, (b) 5 h, and (c) 8 h

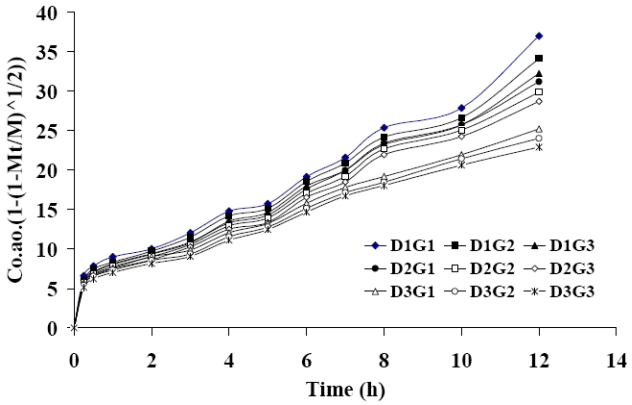



**Fig. 4.** Hopfenberg plots for DCL matrix tablets

Fig. 3 illustrates the response surface plots showing the effect of guar gum granules and matrix granules proportions on percentage of drug release at 2, 5, and 8 h ($Q_2$, $Q_5$ and $Q_8$), respectively. The plots were drawn using *SigmaPlot 11.0* software (Systat Software, Inc., San Jose, CA). Three parameters were considered for the preparation of response surface plots including proportion of DCL matrix granules, proportion of guar gum granules and percentage of drug release at specified times. These plots show the effect of guar gum content in both the layers, DCL matrix layer and guar gum layer, on drug release from triple-layer matrix tablets at specified times.

### *Kinetics of drug release*

The dissolution data of batches were fitted to zero-order, first-order, Higuchi, Hixson-Crowell, Korsmeyer-Peppas, Weibull, and Hopfenberg models. Hopfenberg plots are shown in Fig. 4. The linearization parameters are shown in Table 5. The average $r^2$ of all batches was used to select best fit model.

### *Stability studies*

D3G3 was selected for reference in order to calculate similarity factor ($f_2$). After six months of applied stability conditions D3G3 (D3G3*) showed the similarity factor 83.64.

## DISCUSSION

### *Preparation oftriple-layer matrix tablets*

This investigation uses guar gum as a hydrophilic matrix carrier in matrix tablets. It has been reported that guar gum has poor flow character and low compressibility (19). Here triple-layer matrix tablets incorporate a larger proportion of guar gum. Hence, to improve flow characteristics, low compressibility and to accommodate larger portion of guar gum, DCL matrix granules and

**Table 5.** Linearization parameters of DCL release from matrix tablets

| Model and Parameters | | Formulation code | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | **D1G1** | **D1G2** | **D1G3** | **D2G1** | **D2G2** | **D2G3** | **D3G1** | **D3G2** | **D3G3** |
| Zero-order | $K_0$ (%h$^{-1}$) | 6.8117 | 6.7858 | 6.7178 | 6.6196 | 6.5706 | 6.4848 | 5.8910 | 5.7974 | 5.7067 |
| | $r^2$ | 0.8915 | 0.9006 | 0.9082 | 0.9040 | 0.9097 | 0.9141 | 0.8924 | 0.8976 | 0.9001 |
| First-order | $K_1$ (h$^{-1}$) | 0.0991 | 0.1033 | 0.1055 | 0.1031 | 0.1056 | 0.1071 | 0.0983 | 0.1002 | 0.1022 |
| | $r^2$ | 0.9256 | 0.9189 | 0.9249 | 0.9323 | 0.9299 | 0.9325 | 0.9307 | 0.9304 | 0.9261 |
| Higuchi | $K_H$ (h$^{-1/2}$) | 23.765 | 23.883 | 23.703 | 23.219 | 23.160 | 22.896 | 20.497 | 20.232 | 20.016 |
| | $r^2$ | 0.9784 | 0.9803 | 0.9778 | 0.9736 | 0.9748 | 0.9726 | 0.9793 | 0.9766 | 0.9773 |
| Hixson-Crowell | $K_s$ (h$^{-1}$) | 0.2470 | 0.2231 | 0.2085 | 0.2012 | 0.1922 | 0.1833 | 0.1509 | 0.1442 | 0.1379 |
| | $r^2$ | 0.9468 | 0.9707 | 0.9784 | 0.9818 | 0.9858 | 0.9865 | 0.9950 | 0.9948 | 0.9943 |
| Korsmeyer-Peppas | $n$ | 0.2255 | 0.2550 | 0.2551 | 0.2398 | 0.2715 | 0.2730 | 0.2539 | 0.2574 | 0.2651 |
| | $K_k$ (h$^{-n}$) | 1.6093 | 1.5889 | 1.5721 | 1.5777 | 1.5651 | 1.5514 | 1.5561 | 1.5387 | 1.5218 |
| | $r^2$ | 0.9536 | 0.9668 | 0.9642 | 0.9669 | 0.9508 | 0.9478 | 0.9501 | 0.9463 | 0.9487 |
| Weibull | $Td$ (h) | 5.00 | 5.20 | 5.35 | 5.48 | 5.60 | 5.75 | 6.00 | 6.25 | 6.50 |
| | $\beta$ | 0.5726 | 0.5589 | 0.5465 | 0.5280 | 0.5269 | 0.5202 | 0.4614 | 0.4594 | 0.4606 |
| | $\alpha$ | 2.5134 | 2.5128 | 2.5007 | 2.4552 | 2.4788 | 2.4843 | 2.2857 | 2.3207 | 2.3681 |
| | $r^2$ | 0.8021 | 0.8489 | 0.8590 | 0.8558 | 0.8681 | 0.8708 | 0.8924 | 0.8940 | 0.9020 |
| Hopfenberg | $k_0$ (h$^{-1}$) | 2.4070 | 2.2634 | 2.1610 | 2.0997 | 2.0319 | 1.9595 | 1.6536 | 1.5950 | 1.5392 |
| | $r^2$ | 0.9811 | 0.9887 | 0.9909 | 0.9906 | 0.9922 | 0.9918 | 0.9958 | 0.9948 | 0.9932 |
| Mean Dissolution Time (h) | | 5.00 | 5.20 | 5.35 | 5.48 | 5.60 | 5.75 | 6.00 | 6.25 | 6.50 |

$K_0$, $K_1$, $K_H$, $K_s$, $K_k$, $k_0$: release rate constants, $n$: release exponent (indicative of drug release mechanism), $\beta$: shape parameter, $\alpha$: scale parameter

guar gum granules were made by the wet granulation technique using starch paste as a binder. HPMC was used as a diluent in guar gum granules and DCL matrix granules. HPMC is a widely used release retardant polymer also possesses non-toxic nature and ease of handling (20). On exposure to aqueous fluids or GI fluid, it hydrates to form a viscous gel layer. Drug has to pass through this gel layer by diffusion and/or erosion of the matrix. In prepared DCLtriple-layer matrix tablet, firstly DCL has to diffuse through its own matrix (DCL matrix granule layer) and then through the side layers of guar gum granules. And so drug release was found to be less as the proportion of guar gum in all three layers increased. The presence of HPMC and guar gum ultimately tends to show remarkable effects on the release of drug fromtriple-layer matrix tablets.

### *Evaluation of tablets*

The prepared DCL triple-layer matrix tablets met the acceptance limits for performed evaluation tests. The drug content was found to be uniform among different batches of the tablets. The readings of hardness and friability test prove good binding of granules as wet granulation method was used.

### *In Vitro dissolution studies*

Generally dissolution of matrix tablet involves the penetration of the dissolution medium, hydration, swelling with dissolution/ erosion of the matrix, and the transport of the drug dissolved to the surrounding environment. The release profiles of batches depicted in Fig. 2 shows that the release rate was greatly influenced by the concentration of matrix. A direct relationship observed between the guar gum content in the formulation and DCL release rate. DCL release rate decreased as the guar gum content increased because of increase in gel disentanglement. As the DCL triple-layer matrix tablets come in contact with the phosphate buffer, water taken up by them and become swollen forming a viscous gel layer. The DCL release rate depends on the strength of the gel barrier which depends on the proportion of the guar gum, rate of hydration and viscosity. It is evident from Fig. 3 that higher amount of guar gum in the layers of guar gum granules and in DCL matrix layer retard the DCL release. A more concentrated

gel provides more tortuous and resistant barrier to diffusion which results in slower release of DCL from these matrices. In the initial phase, top and bottom layers over the middle layer were able to delay the interaction of the middle layers with the phosphate buffer pH 6.8 by reducing the surface area available for DCL release and by limiting the dissolution medium penetration rate. During dissolution process, outer layers were progressively eroded and the surface available for DCL release increased. And so, the decrease in the release rate due to the long diffusion path length was compensated by the concurrent increased area for drug release. Afterwards, in the last session of the dissolution process, medium could finally reach the middle layer which become swollen and finally dissolved. The high level of guar gum granules and the higher level of matrix granules favor the preparation of sustained release DCL triple-layer matrix tablets. By selecting the appropriate guar gum granules and DCL matrix granules proportions, the DCL release pattern may be modified.

D3G3 tablet, containing maximum proportion of guar gum in all three layers, was able to deliver the drug at a controlled rate, and hence might be helpful in maintaining therapeutically effective concentrations in systemic circulation for prolonged period of time.

***Kinetics of drug release***

The curve fitting and plotting was performed in *Excel* (Microsoft Software Inc., USA) and *GraphPad Prism*® version 5.02 (GraphPad Software Inc., USA). Linearization of dissolution profiles using the equations in Table 3 is used to characterize the differences found among all batches. The determination coefficient ($r^2$) was used as an indication of the best fit, for each of the models considered. The average $r^2$ of all batches was used to select best fit model. The release rate constant was calculated from the slope of the appropriate plots.

It was found that the *in vitro* drug release from tablets was best explained by Hopfenberg model, as the plots showed the highest linearity ($r^2$=0.9910), followed by Hixson-Crowell ($r^2$=0.9816), Higuchi ($r^2$=0.9550), first-order release model ($r^2$=0.9279), zero-order ($r^2$=0.9020) and Weibull ($r^2$=0.8659). The rate constants values for Hopfenberg model decreased as the content of guar gum increased in matrix granules (Table 5) which indicated that the differing proportion of gum granules mixed with matrix granules could control and modulate the drug release. To fasten the drug release one can reduce the content of guar gum in triple-layer matrix tablet and *vice-versa*. The Hopfenberg model was best fitted and so the release of DCL from triple-layer matrix tablet displayed heterogeneous erosion (15). The magnitude of the release exponent *n* in Korsmeyer-Peppas's equation indicates that the release mechanism is Fickian diffusion, case II transport, or anomalous transport. In this study the values of *n* range between 0.2250 and 0.2730 for all batches, which appears to indicate a classical Fickian diffusion-controlled drug release.

***Stability studies***

The stability studies indicated that batch D3G3 showed no significant changes observed for *in vitro* dissolution studies after six months. D3G3 was found to be stable for the period of six months at 40°C/75% RH.

## CONCLUSION

This study was carried out to develop oral controlled and sustained delivery system for DCL using guar gum as a carrier. The DCL triple-layer matrix tablet, D3G3, containing 87% of guar gum in guar gum layers and 50% of guar gum in DCL matrix granule layer was found to provide the release rate for prolonged period of time. The application of the top and bottom layers on DCL matrix granules layer showed an extended release profile up to 12 h. It can be concluded that guar gum could be a possible potential hydrophilic carrier in the design and development of future oral controlled drug delivery systems.

## ACKNOWLEDGMENT

The authors are thankful to H. B. Gum Industries Pvt. Ltd., Kalol, Gujarat, for the generous gift of pharmaceutical grade guar gum.

## REFERENCES


1. Prasad YVR, Krishnaiah YSR, Satyanarayana S. *In vitro* evaluation of guar gum as a carrier for colon-specific drug delivery. J Control Rel. 1998;51:281-287.
2. Krishnaiah YSR, Satyanarayana S, Prasad YVR, Rao NS. Gamma scintigraphic studies on guar gum matrix tablets for colon-specific drug delivery in healthy subjects. J Control Rel. 1998;55:245-252.
3. Krishnaiah YSR, Satyanarayana S, Prasad YVR, Rao NS. Evaluation of guar gum as compression coat for drug targeting to colon. Int J Pharm. 1998;171:137-146.
4. Krishnaiah YSR, Satyanarayana S, Prasad YVR. Studies on guar gum compression coated 5-amino salicylic acid tablets for colon-specific drug delivery. Drug Dev Ind Pharm. 1999;25:651-657.
5. Gohel MC, Bariya SH. Hypromellose and polyethylene oxide: comparative formulation design oftriple-layer tablets. J Pharm Res. 2010;3:2223-2227.
6. Billa N, Yuen KH, Khader MA, Omar A. Gamma-scintigraphic study of the gastrointestinal transit and *in vivo* dissolution of a controlled release diclofenac sodium formulation in xanthan gum matrices. Int J Pharm. 2000;201;109-120.
7. Billa N, Yuen KH, Peh KK. Diclofenac release from eudragit-containing matrices and effects of thermal treatmen. Drug Develop Ind Pharm. 1998; 24:45-50.
8. Munday DL, Cox PJ. Compressed xanthan and karaya gum matrices: hydration, erosion and drug release mechanisms. Int J Pharm. 2000:203;179-192.
9. Nochodchi A, Farid DJ, Najdfi M, Adrangui M. Studies on controlled-release formulations of diclofenac sodium. Drug Develop Ind Pharm. 1997; 23:1019-1023.
10. Krishnaiah YSR, Karthikeyan RS, Gouri Sankar V, Satyanarayana S. Three-layer guar gum matrix tablet formulations for oral controlled delivery of highly soluble trimetazidine dihydrochloride. J Control Rel. 2002;81;45-56.
11. Syed IA, Narsub ML, Rao YM. *In vitro* release kinetics and bio availability of oral controlled release layered matrix tablets of diltiazem hydrochloride. Int J Drug Dev Res. 2011;3: 234-241.
12. Syed IA, Mangamoori LN, Rao YM. Formulation and characterization of matrix and triple-layer matrix tablets for controlled delivery of metoprolol tartrate. Int J Pharm Sci Drug Res. 2011;3: 23-28.
13. Gohel MC, Bariya SH. Fabrication of triple-layer matrix tablets of venlafaxine hydrochloride using xanthan gum. AAPS Pharm Sci Tech. 2009;10:624-630.
14. Aboelwafa AA, Basalious EB. Optimization and *in vivo* pharmacokinetic study of a novel controlled release venlafaxine hydrochloride three-layer tablet. AAPS Pharm Sci Tech. 2010;11:1026-1037.
15. Costa P, Lobo JMS. Modeling and comparison of dissolution profiles. Eur J Pharm Sci. 2001;13:123-133.
16. Chavda HV, Patel CN. Chitosan superporous hydrogel composite-based floating drug-delivery system: A newer formulation approach. J Pharm Bioall Sci. 2010;2:124-131.
17. Mathews BR. Regulatory aspects of stability testing in Europe. Drug Dev Ind Pharm. 1999;25:831-856.
18. Wagner JG. Interpretation of percent dissolved-time plots derived from *in vitro* testing of conventional tablets and capsules. J Pharm Sci. 1969;58:1253-1257.
19. Ali MS, Singh S, Kumar A, Singh S, Ansari MT, Pattnaik G. Preparation and *in vitro* evaluation of sustained release matrix tablets of phenytoin sodium using natural polymers. Int J Pharm Pharm Sci. 2010;2:174-179.
20. Li CL, Martini LG, Ford JL, Roberts M. The use of hypromellose in oral drug delivery. J Pharm Pharmacol. 2005;57:533-546.