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# DEVELOPMENT AND *IN VITRO* EVALUATION OF SUSTAINED RELEASE MATRIX TABLET FORMULATIOS OF METOPROLOL TARTRATE

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## ABSTRACT

In the present study, metoprolol tartrate (MT) was chosen as a model drug, which is a β1-selective adrenergic blocking agent and is prescribed widely in diverse cardiovascular diseases like hypertension; angina pectoris, arrhythmias and myocardial infarction but because of its short half life (3-4 hrs) and its high water solubility, it was chosen as a suitable candidate for sustained release matrix tablet formulation. It was formulated into matrix tablet using hydrophilic polymers such as hydroxy propyl methyl cellulose (HPMC 15 cps), sodium carboxy methyl cellulose (NaCMC) and guar gum (GG) as release retardants. All the precompressional parameters like angle of repose, Hausner's ratio and Carr's index were found to be within the standard limits. Tablets were evaluated for hardness, friability, thickness, drug content, *in vitro* release, swelling and stability study. The effect of polymer concentration, binary polymer mixture and wet granulation methods on drug release profiles was studied. It was observed that the type of polymer and its concentration has influenced the drug release from matrix tablets**.** Matrix tablets that contained a blend of HPMC and sodium carboxy methyl cellulose successfully sustained the release of metoprolol tartrate for a period of 12 hrs. Precompressional parameters indicated that granules used for preparing tablets were free flowing. Post-compressional parameter like hardness, friability, thickness and drug content were within the acceptable limits. The concentration of metoprolol tartrate was kept constant (100 mg) Formulation containing only a single polymer could not control the release of metoprolol tartrate. The sustained release from sodium carboxy methyl cellulose and hydroxy propyl methyl cellulose combination was due to interaction between ionic polymer and non-ionic polymer, which resulted in favorable increase in the water uptake capacity and gel viscosity leading to a better control over the release of metoprolol tartrate. HC1 and HC2 showed the sustained release of metoprolol tartrate as desired. Model fitting data showed good correlation coefficient with Higuchi's kinetics. The study revealed that the combination of NaCMC and HPMC can be used for the formulation of sustained release matrix tablets of metoprolol tartrate.

**Key words** : Gaur gum, HPMC, Matrix tablets, Metoprolol tartrate, NaCMC, Wet granulation.

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## INTRODUCTION

Oral drug delivery continues to rise in popularity as formulation scientists look for ways to control drug release. The development of sustained release formulations offers some benefits such as controlled administration of a therapeutic dose at the desired delivery rate, constant blood levels of drug, reduction of side effects, minimizing dosing frequency and improved patient compliance[1, 2]. However, developing oral controlled release tablets for water soluble drugs with constant release rate has always been a challenge to the pharmaceutical technologists. Most of these water soluble drugs, if not formulated properly, may readily release the drug at a faster rate and produce a toxic concentration of drug on oral administration. Hence, it is a challenging task to formulate a suitable tablet dosage form for prolonged delivery of highly water soluble drugs.

The most commonly used method of modulating the drug release is to include it in a matrix system. Diffusion controlled polymeric matrix devices have been widely used as drug delivery systems owing to their flexibility to obtain a desirable drug release profile, cost effectiveness and broad regulatory acceptance[3].

Metoprolol tartrate is a cardio selective beta-blocker. It is used in the management of hypertension, angina pectoris, cardiac arrhythmias and myocardial infarction[4]. Metoprolol is readily and completely absorbed from the gastrointestinal tract and having half life 3 to 4 hours[5], necessitating the administration of drug for two or three times daily so as to maintain adequate plasma level of drug. The drug is very soluble in water and hence, judicious selection of rate retarding excipients is necessary to achieve a constant *in vivo* input rate of drug[3].

The present research was directed towards development of sustained release dosage form of metoprolol tartrate in the form of tablets using HPMC, NaCMC and GG by wet granulation method. The tablets were evaluated for different physicochemical parameters such as angle of repose, Carr's index, hardness, thickness, friability, drug content and *in vitro* release. The optimized formulations were subjected to polymer swelling/water uptake studies and their influence on the drug release pattern was studied. The selected formulations were subjected to stability study.

## EXPERIMENTAL

### Materials

Metoprolol tartrate was a gift sample from IPCA Lab. Ltd. (Mumbai-India) HPMC

15cps, NaCMC, Guar Gum was obtained from Signet Chemicals Ltd (Mumbai-India). Magnesium stearate, talc and lactose were procured from SD Fine Chemicals Ltd. (Mumbai-India). All other chemicals were of higher analytical grade.

## Methods

## Preparation of tablets

Metoprolol tartrate, HPMC, NaCMC, guar gum and lactose were passed through 60 mesh screen to deagglomerate the powder materials. 10% w/w Starch paste was used as binder. Sufficient quantity of same is sprinkled over the weighed powder mixture to obtain wet mass. The wet mass was then passed through sieve No. 18 and the wet granules were dried at $60^0$C for 30-40 min[6]. Once dried; the granules were passed through sieve No. 22.Talc and magnesium stearate were finally added as glidant and lubricant. Then these were mixed with granules for 10 mins. The dried granules were compressed using 10 mm round, flat and plain punches on a 10 station tabletting machine. In all formulations, the amount of metoprolol tartrate was kept constant at 100 mg and tablet weight at 320 mg. The formulations of tablets with their codes are shown in Table 1.

**Table 1**

| Formu-lation code | Metoprolol tartrate | HPMC 15 cps | NaCMC | GG | Lactose | Mag. stearate | Talc |
|---|---|---|---|---|---|---|---|
| $H_1$ | 100 | 96 | - | - | 114 | 5 | 5 |
| $C_1$ | 100 | 96 | - | - | 114 | 5 | 5 |
| $G_1$ | 100 | 96 | - | - | 114 | 5 | 5 |
| $HC_1$ | 100 | 95 | 25 | - | 90 | 5 | 5 |
| $HC_2$ | 100 | 80 | 40 | - | 90 | 5 | 5 |
| $HC_3$ | 100 | 65 | 55 | - | 90 | 5 | 5 |
| $HG_1$ | 100 | 108 | - | 64 | 38 | 5 | 5 |
| $HG_2$ | 100 | 76 | - | 96 | 38 | 5 | 5 |
| $HG_3$ | 100 | 44 | - | 128 | 38 | 5 | 5 |
| $HG_4$ | 100 | 12 | - | 160 | 38 | 5 | 5 |

Cont…

| Formulation code | Metoprolol tartrate | HPMC 15 cps | NaCMC | GG | Lactose | Mag. stearate | Talc |
|---|---|---|---|---|---|---|---|
| $CG_1$ | 100 | - | 108 | 64 | 38 | 5 | 5 |
| $CG_2$ | 100 | - | 76 | 96 | 38 | 5 | 5 |
| $CG_3$ | 100 | - | 44 | 128 | 38 | 5 | 5 |
| $HCG_1$ | 100 | 96 | 38 | 38 | 38 | 5 | 5 |
| $HCG_2$ | 100 | 38 | 96 | 38 | 38 | 5 | 5 |
| $HCG_3$ | 100 | 38 | 38 | 96 | 38 | 5 | 5 |

All ingredients are taken in mg per tablet

## Evaluation of powder blend[7 - 10]

The powder blend was evaluated for angle of repose, bulk density, compressibility index and Hausner's ratio.

## Evaluation of tablets[10 - 12]

### Thickness

Thickness of tablets was determined using Vernier caliper. Ten tablets from each batch were used and average values were calculated.

### Weight variation test

To study weight variation, 20 tablets from each batch were weighed using an electronic balance (AW-220, Shimadzu) and the test was performed according to the official method.

### Drug content

Five tablets were weighed individually and triturated. Powder equivalent to the average weight of the tablet was weighed and drug was extracted in water for 6 hours. The solution was filtered through 0.45µ membrane. The absorbance was measured at 274 nm after suitable dilution.

### Hardness

For each formulation, the hardness of 10 tablets were determined using the

Monsanto hardness tester (Cadmach).

## Friability

For each formulation, the friability of 20 tablets were determined using the Roche friabilator. Percentage friability was calculated as follows,

$$F = \frac{\text{Initial weight - Final weight}}{\text{Initial weight}} \times 100$$

## *In vitro* release studies[13, 14]

*In vitro* drug release study for the prepared matrix tablets were conducted for a period of 12 to 14 hrs using USP type II (Electrolab) apparatus at 37 ± $0.5^0$C at 50 rpm speed. The dissolution studies were carried out in triplicate in phosphate buffer of pH 6.8 under sink condition. 5 mL sample were withdrawn at an interval of 1 hr from dissolution medium and replaced with fresh medium to maintain the volume constant. The drug release was analyzed at 274 nm by UV- spectrophotometer. The amounts of drug present in the samples were calculated with the help of appropriate calibration curve.

## Swelling behavior of SR matrix tablet or water uptake studies[15, 16]

The rate of medium uptake by the polymer was determined by equilibrium weight gain method. The study was carried out using prepared matrix tablet formulations. The polymer matrices were accurately weighed and placed in petri dish, containing phosphate buffer (pH 6.8) and maintained at 37 ± $0.5^0$C. At regular intervals, matrix system was withdrawn from petri dish and lightly blotted with a tissue paper to remove excess test liquid and re-weighed. The process is continued for 12 hrs. The percent water uptake, i. e. degree of swelling due to absorbed test liquid was estimated at each time using the following equation –

$$\text{Swelling index} = \{(M_t - M_0) / M_0\} \times 100$$

Where $M_t$ is the weight of the swollen matrix at time t, $M_0$ is the initial weight of the matrix tablet at time t = 0.

## Release kinetics[17]

The dissolution data were examined for models of first order, zero order, Higuchi, Korsemeyer Peppas and Hixon crowell model.

### Stability studies[18]

The stability studies were performed as per ICH guidelines at temperature of $40^0$C and 75% RH using stability chamber for 3 months. The samples were analyzed for drug content.

## RESULTS AND DISCUSSION

### Evaluation of powder blends

The results of angle of repose (< 30) indicate good flow properties of the granules. This was further supported by lower compressibility index values upto (15.3%) and lower Hausner's ratio (1.08 to 1.18) shown in Table 2. These results indicate that granules are good flowing in character.

**Table 2 : Evaluation of granules***

| Formulation code | Angle of repose ( $^0$ ) | LBD ($g/cm^3$) | TBD ($g/cm^3$) | Carr's index (%) | Hausner's Ratio (%) |
|---|---|---|---|---|---|
| $H_1$ | 25.49±0.02 | 0.461±0.05 | 0.50±0.04 | 7.7±0.04 | 1.08±0.01 |
| $C_2$ | 25.71±0.01 | 0.444±0.02 | 0.517±0.02 | 14.16±0.04 | 1.12±0.08 |
| $G_2$ | 27.18±0.05 | 0.461±0.09 | 0.548±0.05 | 14.63±0.02 | 1.17±0.11 |
| $HC_1$ | 25.49±0.05 | 0.444±0.06 | 0.50±0.05 | 11.2±0.06 | 1.12±0.01 |
| $HC_2$ | 25.51±0.01 | 0.461±0.03 | 0.50±0.03 | 7.7±0.05 | 1.08±0.03 |
| $HC_3$ | 26.84±0.01 | 0.461±0.07 | 0.50±0.04 | 7.7±0.07 | 1.08±0.10 |
| $HG_1$ | 25.31±0.05 | 0.454±0.03 | 0.517±0.03 | 12.18±0.05 | 1.13±0.04 |
| $HG_2$ | 28.0±0.04 | 0.458±0.02 | 0.52±0.07 | 12.21±0.03 | 1.13±0.08 |
| $HG_3$ | 29.12±0.07 | 0.458±0.04 | 0.53±0.04 | 14.39±0.06 | 1.16±0.02 |
| $HG_4$ | 26.1±0.04 | 0.428±0.04 | 0.50±0.02 | 14.40±0.03 | 1.16±0.04 |
| $CG_1$ | 24.18±0.02 | 0.444±0.05 | 0.517±0.03 | 14.16±0.02 | 1.16±0.08 |
| $CG_2$ | 25.10±0.01 | 0.441±0.03 | 0.517±0.07 | 14.70±0.07 | 1.17±0.06 |
| $CG_3$ | 27.18±0.06 | 0.461±0.09 | 0.545±0.05 | 15.3±0.05 | 1.18±0.02 |
| $HCG_1$ | 24.21±0.06 | 0.461±0.04 | 0.500±0.05 | 7.7±0.05 | 1.08±0.03 |
| $HCG_2$ | 25.7±0.06 | 0.458±0.09 | 0.521±0.05 | 12.21±0.05 | 1.13±0.09 |

| Formulation code | Angle of repose ( $^0$ ) | LBD ($g/cm^3$) | TBD ($g/cm^3$) | Carr's index (%) | Hausner's Ratio (%) |
|---|---|---|---|---|---|
| $HCG_3$ | 27.15±0.06 | 0.458±0.05 | 0.530±0.05 | 13.74±0.05 | 1.18±0.06 |

*Represents mean ± S. D (n = 3)

## Evaluation of tablets

All the formulations showed uniformity in thickness and weight variation. Good uniformity in drug content was found among different batches of tablets and percentage of drug content was more than 95%. In the present study, the percentage friability for all the formulations was below 1% as shown in Table 3. All the tablet formulations showed acceptable properties and complied with the in-house specifications for weight variation, i. e. post-compressional parameters like weight variation, thickness, drug content, hardness and friability were within acceptable official IP limits.

**Table 3 : Evaluation of tablets***

| Formulation code | Hardness ($Kg/cm^2$) | Thickness (mm) | Friability (% w/w) | Deviation in wt. variation test (%) | Drug content (%) |
|---|---|---|---|---|---|
| $H_1$ | 4.20±0.22 | 3.16±0.16 | 0.75±0.02 | 3.584±0.09 | 99.10±0.02 |
| $C_2$ | 4.0±0.35 | 3.52±0.21 | 0.73±0.12 | 3.125±0.04 | 98.26±0.15 |
| $G_2$ | 3.95±0.15 | 3.57±008 | 0.81±0.07 | 3.223±0.05 | 97.59±0.08 |
| $HC_1$ | 4.5±0.29 | 3.57±0.21 | 0.71±0.14 | 3.712±0.07 | 99.22±0.07 |
| $HC_2$ | 4.6±0.22 | 3.41±0.18 | 0.81±0.19 | 2.989±0.06 | 99.45±0.14 |
| $HC_3$ | 4.0±0.18 | 3.09±0.11 | 0.83±0.12 | 3.604±0.07 | 99.45±0.11 |
| $HG_1$ | 4.0±0.09 | 3.56±0.12 | 0.66±0.12 | 3.816±0.06 | 96.64±0.12 |
| $HG_2$ | 4.10±0.04 | 3.54±0.08 | 0.54±0.08 | 3.215±0.02 | 99.70±0.18 |
| $HG_3$ | 4.2±0.05 | 3.41±0.11 | 0.61±0.11 | 2.965±0.11 | 97.82±0.09 |
| $HG_4$ | 4.0±0.08 | 3.20±0.06 | 0.77±0.12 | 3.712±0.07 | 97.63±0.18 |
| $CG_1$ | 4.0±0.06 | 3.16±0.14 | 0.76±0.14 | 3.105±0.16 | 100.41±0.18 |
| $CG_2$ | 4.05±0.29 | 3.46±0.12 | 0.81±0.19 | 2.864±0.18 | 100.3±0.1 |

Cont…

| Formulation code | Hardness (Kg/cm$^2$) | Thickness (mm) | Friability (% w/w) | Deviation in wt. variation test (%) | Drug content (%) |
|---|---|---|---|---|---|
| $CG_3$ | 4.0±0.14 | 3.54±0.08 | 0.82±0.09 | 3.122±0.16 | 95.95±0.09 |
| $HCG_1$ | 4.2±0.05 | 3.3±0.06 | 0.75±0.13 | 3.792±0.07 | 97.28±0.08 |
| $HCG_2$ | 4.15±0.04 | 3.1±0.11 | 0.73±0.12 | 3.812±0.06 | 97.35±0.12 |
| $HCG_3$ | 4.0±0.08 | 3.4±0.08 | 0.83±0.12 | 3.212±0.07 | 98.81±0.03 |

*Represents mean ± S. D (n = 3)

## Dissolution study

The metoprolol tartrate matrix tablets composed of single polymer like HPMC, NaCMC and guar gum shown in Fig. 1 were not able to control the drug release for 12 hrs. Because of rapid drug release, there may be chances of toxicity and hence, there is a need to use combination of two or more polymers.

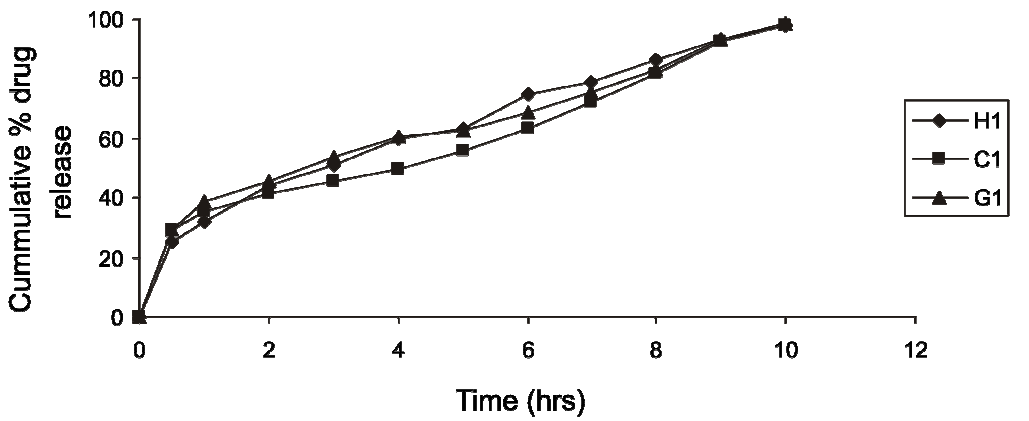


**Fig. 1 : Dissolution profile of metoprolol tartrate matrix tablet of HPMC, NaCMC and guar gum polymer**

The dissolution profile for combination of HPMC and NaCMC i. e. HC1, HC2, HC3 is shown in Fig. 2. HC1 formulation retards the drug releases for 13 hrs. This formulation was able to release 96.70% drug and our dose of the drug is 100 mg that means about 96 mg of drug is released. Where as HC2 and HC3 retards the drug release for 14 hrs and the percent of drug release is 96.42 % and 94.30 %, respectively.

This could be due to swelling as well as erosion of the polymer occuring simultaneously. Both of them contribute to the overall drug release rate. From the dissolution profile of this combination, it is clear that increasing the NaCMC content of SR tablets prolonged the dissolution time. This could be due to CMC decreases water uptake and erosion of the tablet in dissolution medium, which describes the slower release with increasing CMC concentration. The release about 90 % in 12 hrs of HC1 formulation may be due to less amount of NaCMC than the HC2 and HC3 formulations and also due to lactose, which acts as channeling agent, creating pores to the matrix system. These polymer characteristic gives rise to more drug release. The NaCMC and HPMC tablets achieved the highest degree of hydration, which indicate that the ionic interactions between the cellulose ethers increased the water uptake capacity to a greater extent.

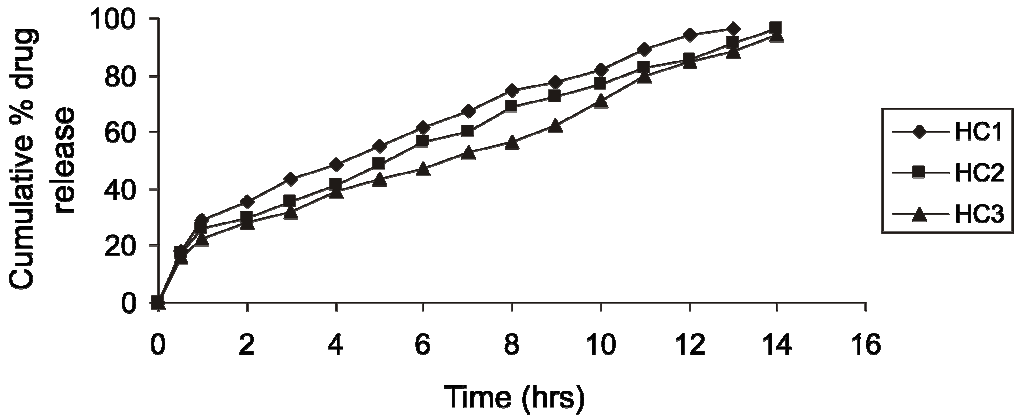


**Fig. 2: Dissolution profile of HPMC + NaCMC formulations**

The control release above 12 hrs was seen with formulation containing combination of NaCMC and HPMC. The slower release from this combination was due to interaction between NaCMC chain and HPMC chain. The capacity of NaCMC to form hydrogen bonds with the hydroxyl group of HPMC led to a synergistic effect on gel viscosity that explains the better control of these polymers on the release of metoprolol tartrate.

The dissolution profile of combination of HPMC and guar gum is shown in Fig. 3. The effect of change of amount of polymers is clearly seen in the dissolution pattern of metoprolol tartrate release from matrices. The percent of metoprolol tartrate released from this combined formulation in 12 hrs is as follows –

HG1 (20 % guar gum) -- 73.32 %, HG2 (30 % guar gum) -- 68.10 %

HG3 (40 % guar gum) -- 67.18 %, HG4 (50 % guar gum) -- 61.03 %

From the above data, it is clear that as the concentration of guar gum was increased, the percent of metoprolol tartrate released is decreased. This is due to formation of thicker layer, which is resistant to the drug release. The actual reason behind this slower release is nature of guar gum on exposure to dissolution fluids, which gets hydrated and forms a viscous gel layer that slows down further seeping-in of dissolution fluids towards the core of the matrix tablet. In all the formulations of guar gum, this viscous gel layer is formed but the strength of this formed gel layer around the matrix tablet is different that depends on several factors such as particle size, force of compression, presence of other excipients, viscosity of polymer, solubility of the drug, etc.

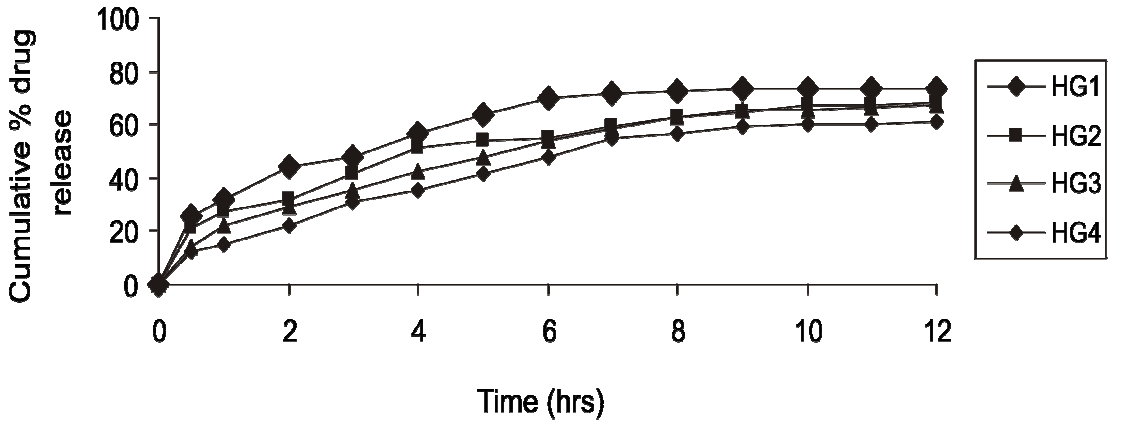


**Fig. 3 : Dissolution profile of HPMC + Guar gum formulations**

The dissolution profile of combination of NaCMC and guar gum is shown in Fig. 4. The percent of metoprolol tartrate released from this combined formulation in 12 hrs is as follows –

CG1 (20 % guar gum) -- 85.60 %, CG2 (30 % guar gum) -- 78.54 %,

and CG3 (40 % guar gum) -- 73.32 %.

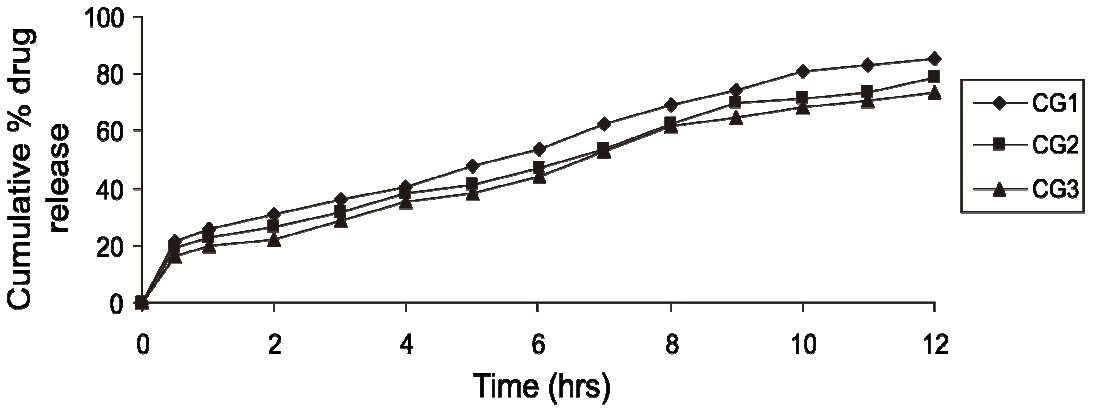


**Fig. 4 : Dissolution profile of NaCMC + Guar gum formulations**

In CG1 formulation, guar gum content is only 20 %. When this guar gum matrix tablet came in contact with dissolution medium, it takes up medium into the system, which is responsible for dissolution of active constituent. Then drug diffused out of the system formulation but due to less guar gum less, viscous gel layer is formed. This gel layer becomes more viscous, when guar gum content is more.

Because of above reasons, the difference in drug release pattern is seen in CG1, CG2 and CG3 formulations of metoprolol tartrate matrix tablet.

All the polymers in combination with varying proportion were used in the preparation of metoprolol tartrate matrix tablet and the dissolution profile is shown in Fig. 5. The percent of metoprolol tartrate released from this combined formulation in 13 hrs is as follows –

HCG1 -- 60.98 %, HCG2 -- 66.47% and HCG3 -- 57.31 %

The drug release is slow because of combination of all the polymers. All the formulations were able to retard the drug release for 13 hrs. The entire tablets retained their physical integrity till the end of the 13 hrs dissolution study.

Dosage form, which can release 80 – 100% of drug in about 8-12 hours, is considered to be a better formulation because the transit time in GIT is around 8-12 hours in the absence of any special gastro retentive methods. The matrix tablets cannot reside in small intestine beyond 12 hours. Therefore, we presume that dosage form, which releases

most of the drug in 12 hrs is a better formulation. Based on the dissolution pattern of all the formulations, the better formulation was HC1 and HC2.

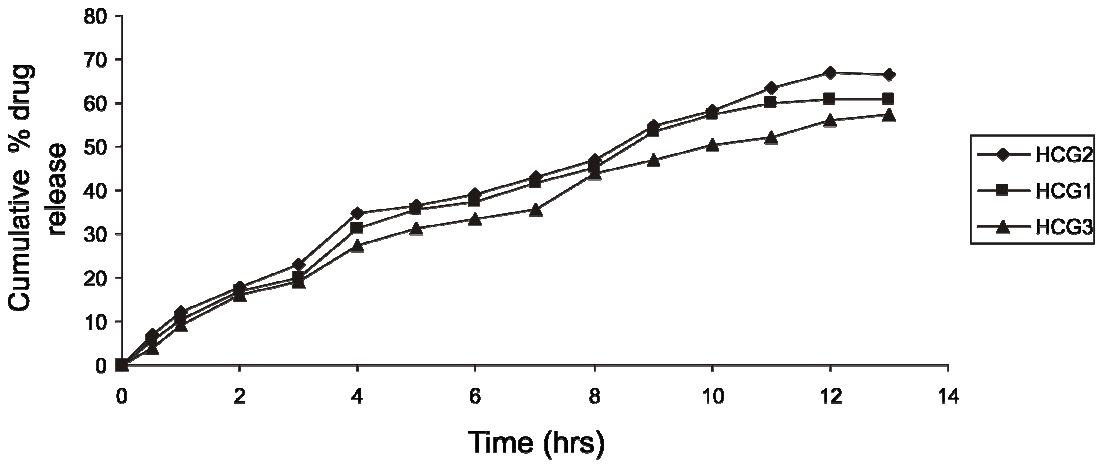


**Fig. 5 : Dissolution profile of HPMC + NaCMC + Guar gum formulations**

## Swelling study

The swelling behavior of HC1, HC2 and HC3 is shown in Fig. 6**.** The swelling behavior of various polymer blends was analyzed to compare their water uptake capacity. The result of swelling study indicate that swelling index value is HC1 > HC2 > HC3. It may be due to increase in content of NaCMC from HC1 to HC3 as shown in Table 1. Hydrophilic polymers have been well known to retard the drug release by swelling in aqueous media. In general, because the drug core of polymer tablets is glassy, the drug contained in them cannot diffuse unless swelling takes place. On swelling, drug molecules dissolve in water and are released by diffusion. The process of swelling, erosion and drug release can occur simultaneously and are interconnected. A polymer ability to retard the drug release rate is related to its viscosity.

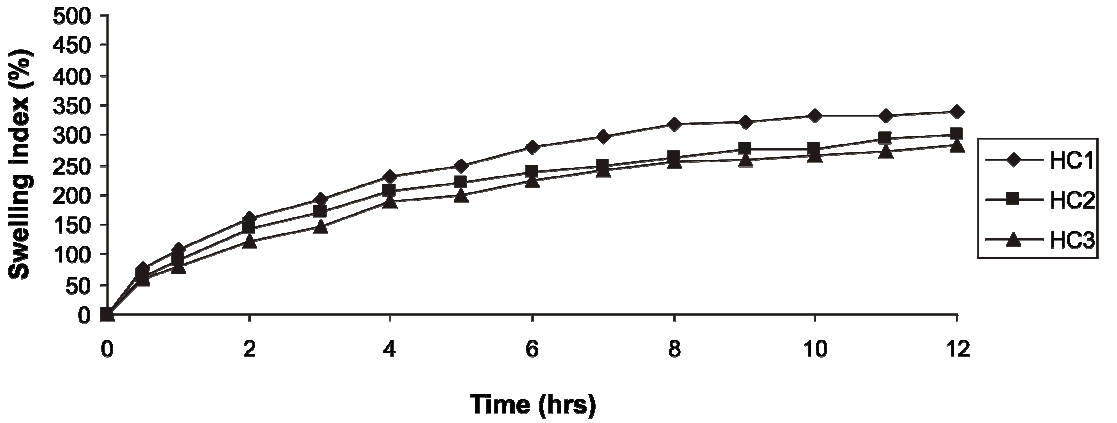


**Fig. 6 : Swelling behaviour of HPMC + NaCMC formulations**

## Release kinetics

The dissolution data were examined for models of first order, zero order, Higuchi, Korsemeyer Peppas and Hixon Crowell model (Table 4). The derived correlation coefficient ($r^2$) indicated good fit of Higuchi model suggesting that diffusion is the predominant mechanism limiting drug release. For all formulations containing HPMC, NaCMC, Guar gum and their combination, the n values were around 0.5 except HCG1, HCG2 and HCG3. These values are closely approximate with n = 0.5 indicating Fickian diffusion. This was also further confirmed with good correlation coefficient found in all formulations with Higuchi's kinetics. The small deviation from n values from its actual value may be because of association of diffusion and erosion of polymer, simultaneously.

**Table 4 : Release kinetics**

| Formulation code | Zero order | First order | Higuchi | Korsemeyer-peppas | Hixon-Crowell |
|---|---|---|---|---|---|
| H1 | 0.8792 | 0.9303 | 0.9371 | 0.9953 n = 0.4569 | 0.9783 |
| C1 | 0.8814 | 0.8779 | 0.9747 | 0.9545 n = 0.3928 | 0.9439 |
| G1 | 0.8172 | 0.8931 | 0.9864 | 0.9868 n = 0.3851 | 0.9516 |
| HC1 | 0.9049 | 0.9512 | 0.9969 | 0.9960 n = 0.5035 | 0.9850 |
| HC2 | 0.9346 | 0.9448 | 0.9906 | 0.9878 n = 0.5159 | 0.9844 |

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| Formulation code | Zero order | First order | Higuchi | Korsemeyer-peppas | Hixon-Crowell |
|---|---|---|---|---|---|
| HC3 | 0.9581 | 0.9351 | 0.9751 | 0.9819 n = 0.5293 | 0.9731 |
| HG1 | 0.4976 | 0.8279 | 0.9445 | 0.9860 n = 0.3533 | 0.7543 |
| HG2 | 0.6862 | 0.8976 | 0.9776 | 0.9925 n = 0.3914 | 0.8456 |
| HG3 | 0.8406 | 0.9530 | 0.9938 | 0.9961 n = 0.5006 | 0.9258 |
| HG4 | 0.8889 | 0.9595 | 0.9902 | 0.9915 n = 0.5525 | 0.9419 |
| CG1 | 0.9247 | 0.9860 | 0.9873 | 0.9758 n = 0.4722 | 0.9860 |
| CG2 | 0.9312 | 0.9858 | 0.9834 | 0.9698 n = 0.4750 | 0.9813 |
| CG3 | 0.9483 | 0.9898 | 0.9803 | 0.9734 n = 0.5232 | 0.9852 |
| HCG1 | 0.9592 | 0.9882 | 0.9775 | 0.9958 n = 0.7226 | 0.9828 |
| HCG2 | 0.9928 | 0.9883 | 0.9471 | 0.9986 n = 0.8948 | 0.9937 |
| HCG3 | 0.9446 | 0.9847 | 0.9860 | 0.9917 n = 0.6477 | 0.9757 |

The stability studies performed as per ICH guidelines for a period of 3 months (Table 5) showed no appreciable difference in the extent of degradation.

**Table 5 : Drug content data for stability study of HC1 and HC2 formulations***

| Formulation code | Drug content before storage | Drug content after storage |
|---|---|---|
| HC1 | 99.22 ± 0.07 | 98.95 ± 0.14 |
| HC2 | 99.45 ± 0.14 | 99.35 ± 0.14 |

*Represents mean ± S. D (n = 3)

## CONCLUSION

The ultimate aim of the present study was to prepare sustained release matrix tablets of metoprolol tartrate using hydrophilic polymers like HPMC, NaCMC and guar gum by wet granulation technique. Precompressional parameter indicated that granules prepared with 10% w/w starch paste were free flowing. Postcompressional parameter like hardness, friability, thickness and drug content were within the acceptable limits. Formulation containing only a single polymer could not control the release of metoprolol

tartrate but blend of HPMC and NaCMC successfully sustained the release of metoprolol tartrate for a period of 12 hrs. The swelling behavior of HC1, HC2 and HC3 showed that matrices containing a minimum NaCMC achieve higher swelling index. The controlled release from NaCMC and HPMC combination was due to interaction between NaCMC chain and HPMC chain, which resulted in favorable increase in the water uptake capacity and gel. The drug release mechanisms for formulations were best described by Higuchi's equation. The formulations followed anomalous behaviour.

The study revealed that the combination of NaCMC and HPMC can be used for the formulation of sustained release matrix tablets of metoprolol tartrate.

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