Design of Controlled Release Non-erodible Polymeric Matrix Tablet Using Microwave Oven-assisted Sintering Technique

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ABSTRACT

The objective of the present study was to evaluate the effect of sintering condition on matrix formation and subsequent drug release from polymer matrix tablet for controlled release. The present study highlights the use of a microwave oven for the sintering process in order to achieve more uniform heat distribution with reduction in time required for sintering. We could achieve effective sintering within 8 min which is very less compared to conventional hot air oven sintering. The tablets containing the drug (propranolol hydrochloride) and sintering polymer (eudragit S-100) were prepared and kept in a microwave oven at 540 watt, 720 watt and 900 watt power for different time periods for sintering. The sintered tablets were evaluated for various tablet characteristics including dissolution study. Tablets sintered at 900 watt power for 8 min gave better dissolution profile compared to others. We conclude that microwave oven sintering is better than conventional hot air oven sintering process in preparation of controlled release tablets.

Key words: Controlled release, eudragit S100, sintering

INTRODUCTION

The objective in dosage form design is to optimize the delivery of medication so as to achieve a measure of control of therapeutic effect in the face of uncertain fluctuation in the in vivo environment in which drug release takes place.[1] There are several physical approaches by which the drug releases from a dosage form can be retarded. The majority of oral controlled release systems rely on dissolution, diffusion or both mechanisms to generate slow release of drug to the gastrointestinal (GI) tract. In the diffusion system, the release of a drug is determined by its diffusion through a water insoluble polymer.[2] One such method to achieve controlled release is sintering of the polymer matrix in which a drug is dispersed and which controls drug release by diffusion through the matrix, by erosion of the matrix or by combination of both erosion and diffusion. Sintering is a better way for controlled release because of its less expensive scale up as well as reduced sintering time.[3]

Sintering is defined as the bonding of adjacent particle surfaces in a mass of powder or in a compact by application of heat.[4] Sintering retards drug release mainly by decreasing the porosity of the matrix.[5] This concept in pharmaceutical science is relatively recent but research interest relating to this process has been growing. Sintering
is a simple and economic process to obtain controlled release of drug from the tablet with relatively less quantity of polymer and avoiding the granulation process in tableting. Many researchers have reported the use of the conventional hot air oven sintering process for controlled release of drug from tablets[6] and microwave oven sintering process for ceramic industry.[7]

A survey of the literature revealed the use of ethylene vinyl acetate, eudragit S-100 and eudragit L-100 as sintering polymers.[8] Use of some waxes like compritol and stearic acid is also reported in sintering.[9] Controlled release tablets for thermally stable drugs like rifampicin, theophylline and ketorolac tromethamine by sintering are reported.

Here, we have used microwave oven sintering for controlled release of drug from tablets. It offers several advantages over conventional hot air oven. Uniform heat distribution leads to uniform sintering compared to a conventional hot air oven where sintering occurs at the surface. The time required for sintering is also less so it is more economical than a conventional hot air oven. The contact time of drug with heat is very low compared to a conventional hot air oven with less chances of drug degradation.

In the present study, we have used eudragit S-100 as sintering polymer and propranolol Hydrochloride (HCL) as a model drug for controlled release.

**MATERIALS AND METHODS**

**Materials**

Propranolol HCL, eudragit S-100, talc and magnesium stearate and other ingredients were of laboratory grade and procured from Yarrow Chemical Products, Mumbai, India.

**Methodology**

*Flow properties of polymer-drug powder blend*

The statics angle of repose was measured according to the fixed funnel and freestanding cone method. A funnel with the end of the stem cut perpendicular to its axis of symmetry was secured with its tip 2 cm above a graph paper placed on a flat horizontal surface. Powder was carefully poured through the funnel until the apex of the cone thus formed just reached the tip of the funnel. The mean diameter and the tangent of the angle of repose were determined.

Compressibility on taping was measured with a sample of 25 g placed in a 100 ml graduated cylinder and the occupied volume (Vo) was determined. After 10 and 500 vibrations, occupied volumes were determined and reported as V_{10} and V_{500} respectively. With these data the compressibility index was calculated using the equation: CI = (d_{500} – d_{10}/d_{500}) × 100.[10]

**Preparation of tablets**

From a review of the literature, it was determined that around 25% of polymer is required for controlled release matrix tablet by sintering technique. Hence, in preliminary trials the polymer was taken at 25% of total tablet weight. Propranolol hydrochloride and eudragit S-100 were accurately weighed using Sartorius monopan balance in the required quantity as shown in Table 1. Drug and polymer were mixed by using a mortar pestle initially for 3 min and finally in a glass bottle by tumbling action for additional 3 min. Then the talc (1%) and magnesium stearate (0.5%) were added as glidant and lubricant, respectively, and mixed thoroughly for 2 min. Finally, the powder mass was compressed into tablets using rotary tablet compression machine (Rimek Minipress, Karnavati Engg. Pvt. Ltd, Ahmedabad, India) at room temperature.

**Sintering of tablets**

Sintering of tablets was performed using microwave oven (Intellocook, LG, India). The fluffy matrix tablets were put into a glass beaker and the beaker was closed by using petri dish. Then this assembly was put into the microwave oven. The tablets were irradiated in the microwave oven at different powers (540 watt, 720 watt and 900 watt) for different time durations. Finally, the sintered tablets were carefully removed from the oven and were evaluated for various tablet parameters as well as dissolution study. The prepared tablets were also sintered using hot air oven at 80°C for 90 min.

**Weight variation test**

Twenty tablets were selected at random, weighed and the average weight was calculated. Not more than two of the individual weights should deviate from the average weight by more than 5%.

**Friability**

For each formulation, pre-weighed tablet samples (20 tablets) were placed in the friabilator (Electrolab, Mumbai, India) which was then operated for 100 revolutions. The tablets were dedusted and reweighed. Conventional compressed tablets that lose <0.5 to 1% of

| Table 1: Composition of propranolol hydrochloride tablets |
|---------------------------------------------------------|
| Ingredients                                             | Quantity |
| Propranolol HCL                                         | 80 mg    |
| Eudragit S-100 (%)                                      | 25       |
| Magnesium stearate (%)                                  | 0.5      |
| Talc (%)                                                | 1        |
their weight are considered acceptable. For sintered tablets the friability was almost negligible [Table 2].

**Hardness**

Hardness of tablet was determined before and after sintering using Pfizer hardness tester (Type 0-12 Janki, India). Hardness of sintered tablets is reported in Table 3.

**Drug content determination**

Twenty tablets were weighed and powdered in a glass mortar. Quantity of powder equivalent to 20 mg of propranolol HCl was accurately weighed and transferred in a 100 mL volumetric flask containing 20 mL of water. The flask was shaken for 10 min and 30 mL of methanol was added. The flask was shaken for an additional 10 min. Finally, the volume was made up to the mark with methanol. The solution was filtered through a 0.45 μ filter and was analyzed by Ultraviolet/Visible Spectrophotometer (UV-1800, Shimadzu, Kyoto, Japan) at 290 nm.

**Fourier transfer infrared spectroscopy**

Fourier transfer infrared (FTIR) spectra of propranolol HCl, eudragit S-100, a physical mixture of propranolol HCl; eudragit S-100 (3:1) before and after heat treatment were recorded using KBr mixing method on FTIR instrument available at the central instrument laboratory of the institute (FTIR-1700, Shimadzu, Kyoto, Japan).

**In vitro dissolution rate study**

The in vitro dissolution study was conducted for all the sintered tablet formulations using United States Pharmacopoeia (USP) Type I dissolution test apparatus (Electrolab, Mumbai, India). Dissolution test was carried out for a total period of 12 h, using 0.1 N HCL (900 mL) as dissolution medium for the first 2 h, and pH 6.8 phosphate buffer for the rest of the time period. At an appropriate time interval, 5 ml sample was withdrawn and replaced with same volume of the fresh dissolution medium. The absorbance of this sample was measured at 290 nm against blank using Shimadzu UV-1800 double-beam spectrophotometer to determine the amount of propranolol hydrochloride released from the tablets.

**Kinetic modeling of dissolution data**

To determine the release kinetics of the drug, various mathematical models were applied like Higuchi diffusion model,[11] Korsmeyer-Peppas model,[12] Hixon-Crowell model,[13] zero order model and first order model. Correlation coefficient ($r^2$) and diffusion coefficient (d) of these models are mentioned in Table 4.

**RESULTS AND DISCUSSION**

Pharmaceutical industries need to characterize the flow property of the powder that makes it possible to estimate their suitability for the directly compressible excipients. In this work we have used some of these tests. Angle of repose and compressibility index on tapping were used for characterizing the flow property of the powder. These tests are used routinely to characterize the bulk solid before compression to optimize flow property in the experimental formulation. Angle of repose and compressibility index

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### Table 2: Tablet parameters

| Batch | Content uniformity (%) | Weight variation (mg) | Friability (%) |
|-------|------------------------|-----------------------|---------------|
| NST   | 94                     | 100 ± 3.0             | 0.06          |
| MOST1 | 95                     | 100 ± 2.5             | 0.02          |
| MOST2 | 94                     | 100 ± 3.0             | 0.02          |
| MOST3 | 95                     | 100 ± 2.0             | 0             |
| HOST  | 78.8                   | 100 ± 2.5             | 0.01          |

NST: Non-sintered tablets, MOST1: tablets sintered at 540 watt power for 15 min with microwave oven, MOST2: tablets sintered at 720 watt power for 10 min with microwave oven, MOST3: tablets sintered at 800 watt power for 8 min with microwave oven, HOST: tablets sintered at 80°C for 90 min with hot air oven.

### Table 3: Hardness of tablets at different power in kg/cm²

|          | NST | MOST1 | MOST2 | MOST3 | HOST |
|----------|-----|-------|-------|-------|------|
| 2.8      | 3   | 3.7   | 4.3   | 3.9   | 4    |
| 2.9      | 2.9 | 3.6   | 4.3   | 3.8   |      |
| 2.8      | 2.9 | 3.7   | 4.4   | 4     |      |
| 2.7      | 3   | 3.7   | 4.3   | 4.2   |      |
| 2.9      | 3   | 3.8   | 4.5   | 3.9   |      |

NST: Non-sintered tablets, MOST1: tablets sintered at 540 watt power for 15 min with microwave oven, MOST2: tablets sintered at 720 watt power for 10 min with microwave oven, MOST3: tablets sintered at 800 watt power for 8 min with microwave oven, HOST: tablets sintered at 80°C for 90 min with hot air oven.

### Table 4: Kinetic treatment of the release data from sintered tablets

| Model                  | MOST1 | MOST2 | MOST3 | HOST |
|------------------------|-------|-------|-------|------|
|                        | $r^2$ | n     | K     | $r^2$ | n     | K     | $r^2$ | n     | K     | $r^2$ | n     | K     |
| Zero order             | 0.85  | 0.91  |       | 0.92  | 0.86  |       |
| First order            | 0.80  |       | 0.92  | 0.85  | 0.80  |       |
| Higuchi                | 0.92  | 0.96  |       | 0.95  | 0.92  |       |
| Korsmeyer Peppas       | 0.95  | 0.29  | 0.52  | 0.97  | 0.33  | 0.46  | 0.96  | 0.31  | 0.46  | 0.94  | 0.31  | 0.44  |
| Hixon Crowell          | −0.80 | −0.87 | −0.82 |       |       |       |       |       |       |       |       |       |

NST: Non-Sintered Tablets, MOST1: tablets sintered at 540 watt power for 15 min with microwave oven, MOST2: tablets sintered at 720 watt power for 10 min with microwave oven, MOST3: tablets sintered at 800 watt power for 8 min with microwave oven, HOST: tablets sintered at 80°C for 90 min with hot air oven.
of powder mixture were found to be 27.23° and 15%, respectively which indicates better flow.

Tablets from all formulations passed the test for weight uniformity. Not more than two tablets differed from the average weight by more than 5% and no tablet differed by more than 10%. Tablets of all formulations passed the test for friability. The hardness of tablets before and after sintering is shown in Table 3. The results indicate that as the power of sintering increases hardness increases. The very low hardness obtained when the tablets were sintered at low power indicates that the main forces holding the particles together are probably Van der Waals and mechanical forces due to interlocking of irregularities on the surfaces of the particles. Increasing the power increased the tablet hardness probably due to the fusion of polymer granules or formation of a welded bond between particles. FTIR study revealed neither drug degradation nor any interaction between drug and the sintering polymer as evident from the FTIR spectra [Figures 1-4].

Sustained drug release was observed from the sintered tablet matrices during dissolution study compared to non-sintered tablets [Figure 5]. From the preliminary studies of sintering and subsequent dissolution it was found that sintering at a power less than 540 watt was not sufficient to sustain the drug release. The power for sintering was gradually increased from 540 watt to 900 watt. The time required for effective sintering at 540 watt was 15 min and was decreased as the power was increased. Sintering at 900 watt for 10 min resulted in browning of the tablets. Hence, the optimum time of 8 min was selected for sintering at 900 watt. Higher power options were not considered as that may cause excessive heating leading to degradation. From Figure 5 it is also evident that hot air oven-sintered tablets show similar sustained drug release as microwave-sintered tablets. The drug content in the tablets sintered using hot air oven was 78.8% [Table 2] indicating drug degradation.

At the end of 12 h, the shape of matrices was not disturbed suggesting that the release of the drug is controlled by diffusion from the matrices. The diffusion-controlled drug release was also supported by the kinetic of release data as the data were fitted to the Higuchi diffusion model [Table 4]. Higuchi has described the drug release mechanism from matrix dosage forms using the equation: \( Q = \left[D \left(2W-C_s \right) C_s t \right]^{1/2} \). In the equation, \( D \) is the diffusion


Figure 5: Comparative dissolution profile of tablets (NST= Non-sintered Tablets, MOST₁ = tablets sintered at 540 watt power for 15 min with microwave oven, MOST₂ = tablets sintered at 720 watt power for 10 min with microwave oven, MOST₃ = tablets sintered at 800 watt power for 8 min with microwave oven, HOST = tablet sintered at 80°C for 90 min with hot air oven)

Coefficient of the drug in the matrices, \( W \) is the total amount of the drug per unit volume of the matrices, \( C_s \) is the solubility of the drug in the matrices and \( t \) is the drug release time. When \( W >> C_s \), the above equation can be simplified to: \( Q = [2WDC_s t]^{1/2} \). This equation indicates that the amount of drug release is proportional to the square root of time for the diffusional release of a drug from the matrix type system. The linear correlation coefficient of the slope shown in Table 4 indicates that the drug release from the eudragit S-100 polymeric matrix follows the Higuchi diffusion model. It had been reported that the eudragit S-100 matrices sintered at increased power might result in a greater extent of sintering due to firmness between eudragit S-100 particles. To gain some insight into the drug release mechanism, a very simple and semi-empirical equation to describe the drug release from the polymeric system, the power law (Korsmeyer-Peppas model, \( M_t / M_\infty = K t^n \)) was also applied. The value of the diffusion exponent obtained was <0.5 indicating Fickian diffusion of the drug from sintered tablet matrices.

**CONCLUSION**

Among the different strategies employed for the design of a controlled release dosage form, sintering technique for the preparation of polymer matrices for the controlled release of propranolol is an alternative technique. This new method for controlling the release rate has been developed and tested here using microwave oven for sintering which gives more uniform heat distribution with less time required than a conventional hot air oven.

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**REFERENCES**

1. Rao SB, Seshasayana A, Kumar RN. Studies on release of rifampicin from sintered matrix tablets. Indian J Pharm Sci 2001;63:371-8.
2. Umamaheshwari RB, Jain NK. Controlled and novel drug delivery systems. In: Jain NK, editor. Pharmaceutical product development. 1st ed. New Delhi: CBS publishers and distributors; 2006. p. 419-55.
3. Rao SB, Seshsayana A, Himasankar K. Design and evaluation of ethylene vinyl acetate sintered matrix tablets. Indian J Pharm Sci 2003;65:496-502.
4. Luk CI, Jane HL. Sintering in pharmaceutics. In: Swarbrick J, Boylan JC, editors. Encyclopaedia of pharmaceutical technology. 2nd ed. New York: Marcel Dekker Inc; 1996. p. 87-101.
5. Rao MR, Ranpise AA, Thakri KC, Borate SG, Parikh GN. Effect of processing and sintering on controlled release wax matrix tablets of ketorolac tromethamine. Indian J Pharm Sci 2009;71:538-44.
6. Rao SB, Sankar KH, Sirisha BS. Design and evaluation of eudragit RL100 sintered matrix tablets. Indian J Pharm Sci 2004;66:202-7.
7. Kartz JD. Microwave sintering of ceramics. Annu Rev Mater Sci 1992;22:153-76.
8. Kondaiah A, Prakash K. Design of controlled release non-erodible polymeric matrix tablets of theophylline using sintering technique. Indian J Pharm Sci 2002;64:239-43.
9. Zhang Y, Schwartz B. Effect of processing method and heat treatment on formulation of wax matrix tablet. Pharm Dev Technol 2001;6:131-44.
10. Singh R, Podda SS, Chivatte A. Sintering for controlling release from pellets. AAPS PharmSciTech 2007;8:E9-1.
11. Higuchi T. Mechanism of sustained action medication, theoretical analysis of rate of release of solid drugs dispersed in solid matrices. J Pharm Sci 1963;52:1145-9.
12. Hixon AW, Crowell JH. Dependence of reaction velocity upon surface and agitation. Ind Eng Chem 1931;23:293-31.
13. Korsmeyer R, Gurny R, Peppas N. Mechanism of solute release from porous hydrophilic polymers. Int J Pharm 1983;15:25-9.

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