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Use of Sintering Technique in the Design of Controlled release Stomach Specific Floating Drug Delivery Systems

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ABSTRACT: Sintering technique is a relatively new, convenient, economic process for the design of controlled release dosage form. Sintering means fusion of particles or formation of welded bonds between particles of polymer. The sintering technique has been used for the fabrication of matrix tablet for sustained release and retardation of release of drug from various systems. The sintering condition markedly affected the drug release characteristics from the sintered tablets. Among the several physical approaches employed for the design of controlled release dosage form, sintering of polymeric matrix in which a drug is dispersed is an alternative technique. The challenges associated with floating drug delivery system can be overcome by upcoming novel sintering technique. This review article explains the various aspects of sintering technique and also highlighted some research work on floating drug delivery systems prepared by sintering technique.

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INTRODUCTIONS:

The concept of sintering in pharmaceutical sciences is relatively new, but the research interests related to this process have been growing continuously. In powder metallurgy, sintering is defined as bonding of adjacent particle surfaces in a mass of powder or in compact, by the application of heat. Conventional sintering technique involves the heating of compact at a temperature below the melting point of the solid constituent in controlled environment under atmospheric pressure. Historically, sintering is a method used to fabricate parts from metals,

ceramics and glass. Microwave sintering, plasma-activated sintering and laser sintering is the more recent advance in sintering technologies [1,2].

In the pharmaceutical science, sintering has been described as the mechanism for the strengthening of the mechanical properties of consolidated pharmaceutical powder at elevated temperature, for solid-bond formation during tablet compression, and for thermal curing of polymer-latex film coating .The sintering process has been use for the fabrication of sustained- release matrix tablets for the stabilization the dug permeability of film coatings derived from various pharmaceutical lattices [3,4].

SINTERING METHODS:

Sintering means fusion of particles of polymer. There are two types of sintering methods, namely solvent casting (Acetone saturation) and thermal sintering method [5].

Acetone saturation method:

This method involves exposure of compressed tablets to acetone vapor in desiccator. The lower chamber of the desiccator was filled with acetone, closed and kept aside for saturation. After saturation the compressed tablets were taken in Petri dishes and place over a wire mesh which is kept above the lower chamber of the desiccator containing acetone. The desiccator is made air tight by closing the lid with the help of wax [6]. The acetone vapors in the saturated desiccator enter the pores of tablets; solubilise the surface of the polymer which results in the fusion of particles, thus bringing about sintering. After exposure for predetermined time intervals, the tablets were removed from the desiccator, dried at a ambient temperature to evaporate adhering free acetone for 24 h and were finally dried in a vacuum desiccator over fused calcium chloride for 24 h [7].

Thermal sintering method:

Thermal sintering technique is a method of heating polymeric matrix in a sintering furnace below the melting point of the solid constituents until its particles adhere to each other. In this process, polymer particles undergo fusion or formation of welded bonds between each particle. The thermal sintering method involves fusion of polymer particles or formation of welded bond between particles by exposing the polymer matrix to the temperature above the glass transition temperature of the polymer. The entrapment of drug particles in the welded bond leads to controlled release of drug [5,8].

Thermal sintering involves the heating of a compact at a temperature below the melting point of the solid constituents in a controlled environment under atmospheric pressure. The exposure of the dosage form to the sintering temperature softens the polymer matrix and leads to the formation of welded bonds. The drug particle gets entrapped in the matrix formed and these results in the controlled release of the active ingredient. Among the different strategies employed for the design of controlled release dosage forms, sintering technique is one of them. [9] It is simple, effective and economical processes to obtain sustain release of drug from the tablet with comparatively less quantity of polymer. This sintering technique is used extensively for sustain release in various dug [10,11].

Sintering concept in the pharmaceutical science is relatively recent .sintering occurs at elevated temperature and involves mainly three principle steps; joining adjacent particles together termed as neck growth formation of interconnecting pore channels termed as densification followed by formation of spherical shape of particles which tends to flow into the pores within it due to the difference between vapor pressure and cross-sectional area of the pore's neck. These stages of sintering result in bonding of the particles together and ultimately in removal of internal porosity, causing external shrinkage and achievement of desirable physical properties [12].

Thermal sintering method V/s. Solvent casting method:

As compared to the solvent casting method the thermal sintering method have the following advantages; reduction processing time, no need of solvent removal, elimination of shrinkage and no adverse effect on the macromolecule because of solvent exposure. However this method is applicable to only those drugs that are resistant to the temperature of exposure and may be the limiting factor for the drugs that get degraded at elevated temperature [12].

THEORY OF SINTERING:

Driving forces for sintering:

The principal driving force for sintering is the reduction of total free energy in the system as a result of the bonding of particles, void-space shrinkage and the consequent decrease in total surface area of the compact. Hence, from the thermodynamic point of view, sintering is a spontaneous process.

A simple two sphere sintering model (Fig 1) was described, based on Laplace's equation, to examine the chemical-potential gradients of the surface of a solid in

regard to the driving forces for sintering. The stress distributed around the neck area is expressed by the following equation 1.

$\sigma = \gamma (-1/r + 1/x)$ ……. (1)

Where γ is the Surface energy of the solid.

As x>>r, the term of 1/x can be neglected and stress is taken as equation 2.

$\sigma = - \gamma / r$ ……. (2)

The negative sign indicates a tensile stress. The corresponding gradient in chemical potential may be as equation 3.

$\mu - \mu_0 = \sigma \Omega = - \gamma \Omega / r$ ……(3)

Where μ is the chemical potential over the convex side of curvature with radius 'r', μ_0 is the chemical potential at adjacent flat surface which is not under stress and Ω is the Atomic volume.

The chemical potential gradients ($\mu - \mu_0$) for the surfaces of the two spheres become the driving force for sintering [1,2,12].

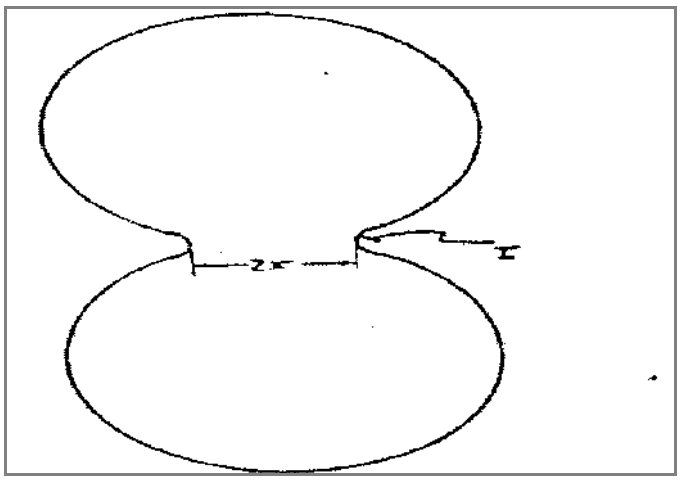

Fig 1. Two-sphere sintering model, showing the diameter (2x) of the neck between the particles and the radius (r) at the end of the neck.

SINTERING MECHANISM:

Sintering in single solid phase:

According to Wretbland and Wuff, the process of sintering in solid phases occurs by combination of two or three material-transport mechanisms [1,2,5,12].

Sintering in solid phases occurs by one of the following material-transport mechanisms:

- Evaporation and condensation.
- Plastic and viscous flow.
- Volume and surface diffusion flow.

According to Wretbland and Wuff, the sintering process is the result of combination of two or three of these mechanisms.

***Evaporation and condensation*:**

The gradient in the chemical potential ($\mu - \mu_0$) between the convex surface and the adjacent flat surface (Fig 1) creates a vapor-pressure gradient that can be described by Gibbs-Thomson equation;

$\mu - \mu_0 = RT (\ln P - \ln P_0)$ ….. (4)

Where, R is the gas constant, T is the absolute temperature, P is vapor pressure over the stressed (curved) surface and P_0 is the Vapor pressure over the unstressed (flat) surface.

Because of these differences in vapor pressure, material evaporates from the flat surface and condenses on the curved surfaces. This mass transfer mechanism is more significant for a substance with a high vapor pressure, particularly at a temperature close to its melting point.

***Plastic and viscous flow*:**

On a surface of a solid with a sufficiently small radius of curvature, the developed stress becomes sufficiently high to provide dislocation via plastic deformation. In the absence of external pressure, plastic flow may contribute to the material transport phenomenon only in the very large stages of sintering. However, when pressure is applied during sintering, such as in a hot-pressing process, plastic flow becomes the predominant mass-transport mechanism.

***Volume and surface diffusion flow*:**

Diffusional flow as a mass-transport mechanism for sintering is based on the concept that a certain concentration of vacancies exists in the lattice of a crystal. Again, considering the two spheres model (Fig 1), the gradient in chemical potential between the highly curved surface and the adjacent flat surface creates a gradient in vacancy concentration.

Sintering in liquid phase [1,2,5,12]:

Sintering in liquid phase occurs by the following material transport stages:

***Rearrangement stage*:**

In the rearrangement stage, densification is brought about by the action of capillary pressure caused by the collapse of melt bridges between particles and by the rearrangement of solid particles sliding over each other.

***Accommodation stage*:**

This stage may be described as the growth of solid particles via a process of dissolution of the smaller particles and their re-precipitation on the larger ones as a result of the differences in solubility of small and large

particles in the liquid phase. Since the solubility of the solid phase in the bulk is relatively low, material is transported from the contact region and re-precipitated in the bulk.

***The solid-state sintering stage*:**

Prolonged exposure of the compacts to the sintering temperature may lead to solid-state sintering, which results in further particle growth in the solid phase and formation of a solid skeleton. In some cases, a rigid skeleton in the solid phase may be formed prior to complete densification.

The formation of this skeleton may interfere with rapid densification by rearrangement.

VARIOUS STAGE OF SINTERING TECHNIQUE:

The alteration of the microstructures within a pharmaceutical compact during sintering is the prevailing factor in determining the release rate of the drug. In the application of this sintering technique to the fabrication of controlled release dosage form, the main research focus has been on the influence of sintering on the alteration of the microstructures in a polymeric matrix and the release of the active ingredients from the matrix. The structural changes within a compact during sintering can be broken down into several stages. Some of which may occur virtually simultaneously. Five different stages [1,3,12] of sintering are illustrated in Fig 2, as detailed below;

Inter-particle Bonding:

The transport of molecules at the point of particle contact leads to the formation of physical bondings and grain boundaries. The initial bondings take place rapidly.

Neck Growth:

Continuing material transport results in the development of a distinct "neck" between particles. The strength of the compact is considerably enhanced at this stage.

Pore-Channel Closure:

The continuing neck growth leads to the closure of some pore channels within the compact, giving rise to isolated pores.

Pore Rounding:

As the neck growth reaches its final stage, the transport of material from the bulk to the neck regions produces a smoothing effect on the pore wall. At this stage, the toughness of the compact is further strengthened.

Pore Shrinkage:

With further sintering, the pores in the compact start to shrink in size and decrease in numbers. This facilitates further densification. This stage involves extensive material transport and the annihilation of vacancies in the compact.

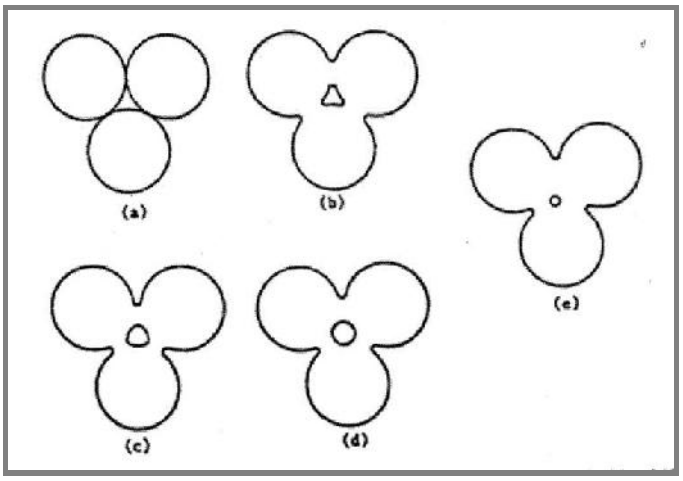

Fig 2. Three-sphere sintering model (a) Original points of contact; (b) Neck growth; (c) and (d) Pore rounding; (e) Pore shrinkage.

GASTRO RETENTIVE FLOATING TABLETS:

Gastro retentive drug delivery system plays a vital role among novel drug delivery systems. Oral sustained release gastro-retentive dosage forms offer many advantages for drugs. The retention of oral dosage forms in the upper GIT causes prolonged contact time of drug with the GI mucosa, leading to higher bioavailability, and hence therapeutic efficacy, reduced time intervals for drug administration, potentially reduced dose size and thus patient compliance [13].

Gastro retentive drug delivery get popularity from last two decades leading to its potential application to improve oral delivery of some important drugs for which prolonged gastro retention can greatly improve their oral bioavailability. GRDDS not only prolong the dosing intervals, but also increase the patient compliance beyond the level of existing controlled release dosage form. The model drug release in control and sustain manners the various approaches are available in the GRDDS like Mucco- adhesive, Hydro dynamically based system, swelling and expanding system, high density system etc. Gastro retentive dosage forms are formulated to be retained in the gastric region for prolonged time and release incorporated drug candidates and thereby enable sustained and prolonged input of the drug to the upper part of the GIT thus leading its optimal bioavailability. Thus, they not only prolong the dosing intervals, but also increase the patient compliance beyond the level of existing controlled release dosage forms. This application

is especially effective in delivery of sparingly soluble and insoluble drugs. Gastro retentive dosage forms greatly improved the pharmacotherapy of GIT [14,15].

RECENT RESEARCH WORK REPORTED ON FLOATING TABLETS PREPARED BY SINTERING TECHNIQUE:

Thermally sintered floating tablets of propranolol HCl:

Meka VS, *et al.* in their work formulated thermally sintered floating tablets of propranolol HCl, and studied the effect of sintering conditions on drug release, as well as their in-vitro buoyancy properties. The results showed that sintering temperature and time of exposure greatly influenced the buoyancy, as well as the dissolution properties. As the sintering temperature increased the floating lag time was found to be decreased, may be due to decreasing porosity. During the sintering process, the void spaces between the particles might decreases and each particle will exposed to surface of gastric fluid quickly, which leads to a decrease in the floating lag time. Similarly as the sintering temperature increased the total floating time was increased, may be due to the formation of strong welded bonds between the particles, which makes tablet intact for a longer period .sintering time was inversely proportional to floating lag time and directly proportional to total floating time. As the sintering temperature and sintering time increases, release of the drug was decreased. The drug retarding property might be due to the formation of the welded bonds by softening of the polymer to which the drug particles might have been entrapped in the matrix formed which results in the controlled release of drug. They concluded that the thermal sintering technique can be used in the design of gastro retentive floating tablets of propranolol HCl with the reduced polymer quantity and with the desired dissolution profile using PEO as a retarding polymer [16].

Gastro Retentive floating matrix tablets of Nicardipine HCl by thermal sintering technique:

Mohanty C, *et al.* in their study prepared thermally sintered floating matrix tables of Nicardipine HCL and studied the effect of sintering conditions on in-vitro dissolution study, in-vitro buoyancy properties, hardness and friability. Floating lag time was found to be decreased with increase in the sintering temperature, which might be due to decreasing porosity. When the tablets were exposed to sintering temperature, the void spaces between the particles if the tablets may be decreased and each particle was exposed to the gastric fluid quickly. As the sintering temperature was increased total floating time was also increased. This is might be attributed to the formation of welded bonds between the particles by softening and fusion of polymer particles, which makes tablet intact for longer period.

The hardness of the sintered tablets were found to be increased with increase in sintering temperature and duration of sintering, may be due to the formation of welded bond among the polymer after sintering condition. Friability of tablets was found to be decreased with increasing sintering time. Hence by using thermal sintering technique friability of tablets can be reduced.

The *in-vitro* dissolution studies shown that the release rate of the drug was inversely related to the sintering temperature and the sintering time. Increasing the temperature or the time of exposure to a particular temperature often decreased the release rate. This was attributed to the slow softening and fusion of polymer particles and formation of welded bond between them. The drug particles are entrapped in the formed matrix which results in the controlled release of drug. It was also observed that the release rate of the drug was decreased as the concentrations of polymer increased, which may be due to increased intensity of air pockets surrounding the jellified tablet surface. The authors concluded that a simple technique of thermal sintering may be used in the design of GRFT of Nicardipine HCL to sustain the drug release, decrease the floating lag time, increase the total floating time, and prolong the gastric residence time and ultimately its bioavailability [17].

Thermally sintered sustained release gastro retentive floating matrix tablets of Atazanavir sulphate:

Mohanty C, *et al*. prepared and evaluated thermally sintered gastro retentive floating matrix tablets of Atazanvir sulphate. Effects of sintering condition were studied on *in vitro* dissolution studies, hardness, friability, floating lag time and total floating time. From the results it was observed that the sintering temperature and the sintering time markedly affected the drug release properties. The release rate of drug was inversely related to the sintering temperature and the sintering time. Increasing the temperature or time of exposure to a particular temperature often decrease the release rate. The drug retarding property might be due to the fusion of polymer granules and formation of welded bonds by softening of polymer to which drug particles may have

been entrapped in the matrix formed which results in the controlled released of drug.

By using sintering technique floating lag time of tablets was found to be decreased with increase in the sintering temperature and total floating time was increased with increase in the sintering the temperature. In addition the hardness was increased with increased in sintering temperature and duration of sintering, where as friability of tablets was found to be decreased with increasing sintering time.

They concluded that a simple technique of thermal sintering may be used in the design of gastro retentive floating tablets (GRFT) of Atazanavir sulphate to sustain the drug release , decrease the floating lag time ,increase total floating time, improve the local action and ultimately its bioavailability [18].

Thermally sintered floating tablets of Propranolol HCl using box-behnken experimental design:

Srikanth MV, *et al.* formulated thermally sintered floating tablets of proparnolol HCl using experimental design (Box Behnken) to study the effect of sintering conditions on the drug release as well as buoyancy properties. Formulations were prepared using for independent variables namely polymer quantity, sodium bicarbonate concentration, sintering temperature and sintering time, whereas floating lag time, and t_{95} are taken as dependent variables. The formulations were prepared by the direct compression method using polyethylene oxide (PEO) as release retarding polymer and were evaluated for in vitro dissolution studies. All the unsintered and sintered tablets passed physicochemical tests concerning the weight variation, assay and friability. The results shown that as the sintered temperature increased, the floating lag time decreased. From the obtained results it was observed that the drug retarding property mainly depends upon the sintering temperature the sintered time. The drug retarding property was directly proportional to the sintered temperature and the sintering time. The drug retarding property might be due to the formation of the welded bonds by softening of the polymer due to which the drug particles might have been entrapped in the matrix formed which results in the controlled release of the drug. From the results it was observed that as the concentration of the polymer increased along with concentration of sodium bicarbonate, the drug release was retarded. This may be due to the increased intensity of air pockets surrounding the jellified surface of the tablet. The increase in the concentration of sodium bicarbonate at constant polymer concentration also retarded the drug release due to the high intensity of the carbon dioxide gas pockets. From the experimental data it is concluded that there was a decrease in the floating lag time, an increase in the total floating time with the duration of exposure to varying temperature. In addition, *in vitro* drug release was retarded with the increase in the duration of exposure to the sintering temperature.

Hence, they concluded that concept of the thermal sintering can be used to reduce the polymer quantity with the desired dissolution profile [19].

Non-effervescent gastro retentive floating matrix tablets of Metronidazole using non effervescent (sublimation and sintering) technique:

Airemwen CO, *et al.* in their work formulated a novel non effervescent gastro-floating matrix tablets of Metronidazole using non effervescent i.e. sublimation and sintering technique. Granules were prepared by wet granulation technique using vary concentration of *Grewia mollis* gum 2,4,6 and 8 % w/w admixed with 1 % w/w acrylate methacrylate copolymer (Eudragit RL100) and extra 2 % w/w batch without addition of Eudragit RL 100. Ammonium bicarbonate (30 % w/w) was used as the sublimating agent. The granules were characterized for micromeritic properties. The granules were compressed at 30 units on the arbitrary scale load of single punch tableting machine and the physicochemical properties were determined. The metronidazole tablet was then sintered at 70 ^{0}C for 12 h. Hardness of the formulated tablets in the various formulation varied form 6.0±0.1 to 7.5±0.1 Kpa indicating good mechanical strength with an ability to withstand physical and mechanical stress while handling, storage and transportation. The loss in total weight of the tablet due to friability in the range of 0.7±0.1 to 0.8±0.1.2 % in all the formulations and the value was less than 1 % which ensures that the formulated tablets were mechanically stable to withstand fracture and abrasion due to handling, transportation and storage. The drug content in the different tablet formulations was uniform and ≤85 % which is within the permissible limits of the British pharmacopoeia.

The result of the *in vitro* buoyancy study shown that all the tablet formulation had no floating lag time (0 s) as they floated instantaneously when placed on the simulated gastric fluid (0.1 N). The mechanism of floating was due to the sublimation of the ammonium

carbonate from the tablets during the sintering (heating) process thereby creating pores in the tablets which enable the tablets to float freely on top of the simulated gastric fluid and the sublimation of ammonium carbonate also reduces the bulk density of the tablet less than that of the simulated gastric fluid thus conferring buoyancy. The drug release from the floating Metronidazole tablet of 2% w/w *Grewia mollis* gum without Eudragit RL 100 showed a faster release of drug content compared to the other batches containing Eudragit RL 100. This is because Eudragit RL 100 helps in maintaining the integrity of the tablet and sustaining the drug release from the tablet formulations. The % maximum release and time to achieve it for Metronidazole tablet were ≥88 % and ≥10 h respectively. The authors concluded that gastro retentive floating non-effervescent matrix tablets of Metronidazole can be formulated using the sublimation and sintering techniques to prolong gastric retention time and subsequently sustain drug release for up to 10 h [20].

Gastro retentive tablets of Glipizide by solvent casting sintering technique:

Seshagiri B, *et al.* designed hydro dynamically balanced drug delivery system for Glipizide using HPMC K_4M and HPMC $K_{15}M$ polymers by solvent casting sintering technique. Various batches of matrix tablets of Glipizide were prepared varying concentration of polymers using direct compression method which were exposed to different time period under saturated acetone vapors system for sintering. Tablet hardness was increased with increase in the sintering time. This ensured good handling characteristics of all batches. Tablets exposed to acetone vapors for a greater period showed the least friability as compared to the tablets that were unsintered. Therefore, by using technique of sintering the friability of tablet can be reduced to a greater extent. The % friability was less than 1 % in all the formulation ensuring that the tablets were mechanically stable. Buoyancy lag times of the formulations were found to decrease as the time of sintering was increased. Form the *in-vitro* dissolution data, it was found that the drug release studies from formulations containing HPMC $K_{15}M$ sintered for 1.5, 3.0 and 4.5 h, the cumulative percentage releases were 88.58, 77.58 and 69.17 % respectively and 93.11 % for unsintered tablet. Formulation containing HPMC K_4M sintered for 1.5, 3.0 and 4.5 h the cumulative percentage release was 96.34, 92.78 and 85.67 % respectively and 99.25 % for unsintered tablets.1.5, 3.0 and 4.5 h, the cumulative percentage release was 89.96 and 82.43 % respectively and 95.05 % for unsintered tablets. The effect of sintering time on the drug release from matrix tablets was evaluated and it was found that the time of sintering is proportional to the amount of drug release. They concluded that by using solvent casting sintering method gastro retentive delivery systems Glipizide can be successfully developed in the form of hydro dynamically balanced tablets to improve the local action ultimately its bioavailability [21].

CONLUSION:

In conclusion, sintering technique adds to the effectiveness of polymers for controlling drug release and provides a significant and expedient method for control release in oral dosage form. Sintering condition markedly affected the drug release properties depending upon the duration and temperature of sintering. The simple technique sintering can be used in the design of gastro retentive floating drug delivery systems to sustain the drug release, decrease the floating lag time, increase total floating time, and improve the local action and ultimately the bioavailability of active medicament. However both the sintering methods i.e. thermal sintering technique and solvent casting methods are having disadvantages; such as thermal decomposition of some drug molecule due to prolonged exposure to higher temperature in case of thermal sintering and adverse effects due to the solvent exposure in case of solvent casting method. But, a better understanding of the theoretical and technical aspects of the sintering process may allow the identification of its specific needs for pharmaceutical manufacturing such as the fabrication of controlled-release polymeric matrix systems. More importantly, an understanding of the ever-growing advancements in new technologies relating to sintering as used in other technical fields may lead to new applications of modern sintering processes to pharmaceutical systems.

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REFERENCES:

1. Luk CL, Jane HL. Encyclopedia of Pharmaceutical Technology. In: Swarbrick J, Boylans JC, editors. Sintering in Pharmaceutics. 2nd ed. New York: Marcel Dekker; 1996. pp. 87-101.

2. Tejaswini SP, Ramdas BR. A review on sintering method in Pharmaceutical sciences. Asian J Pharm Tech, 2014; 4(2): 106-109.
3. Mohanty C. Sintering technique in Pharmaceutical Sciences: A brief review. Int J Pharmatech, 2011; 3(1): 799-806.
4. Bhanja S, Ellaiah P, Mohanty C, Murthy KVR, P Bibhutibhusan, Padhy SK. Design and *in Vitro* Evaluation of Mucoadhesive Buccal Tablets of Perindopril Prepared by Sintering Technique. Int J Pharmatech Res, 2010; 2(3): 1810-1823.
5. Amol RB, Smita SA, Saudagar RB. A review on sintering technique in pharmaceutical sciences. Int J Chemtech Res, 2017; 10(5): 210-215.
6. Dhiraj GS, Amit SP, Roshan PV, Majumdar SH. Formulation and evaluation of matrix tablet of Cefpodoxime proxetil by sintering technique. Am J Pharmtech Res, 2013; 3(5): 338-349.
7. Rao BS, Raju YP, Srinivas L, Seshasayana A. Design and evaluation of Eudragit RL 100 sintered matrix tablet. Indian J Pharm Sci, 2014; 64(2): 202-207.
8. Mohanty C, Subrahmanyam KV. Effect of sintering condition on Physico-chemical parameters and drug release characteristics from polymeric matrix tablet of Atenolol for controlled release. Int J Pharm Sci Res, 2017; 8(9): 1000-1009.
9. Rao BS, *et al*. Studies on release of rifampicin from sintered matrix tablet. Indian J Pharm Sci, 2001; 63(5): 371-378.
10. Patwekar TS, Rode RB. Review on Sintering Method in Pharmaceutical Sciences. Asian J Pharm Tech, 2014; 4(2): 106-109.
11. Amol RB, Smita SA, Saudagar RB. A Review on Sintering Technique in Pharmaceutical Sciences. Int J ChemTech Res, 2017; 10(5): 210-215.
12. Mohanty C, Subrahmanyam KV, Chandana P, Swathi A. Applicability of sintering technique in fabrication of controlled release dosage form. Int J Innovative Pharm Sci Res, 2018; 6(5): 9-20.
13. Garg R, Gupta GD. Progress in controlled gastroretentive delivery systems. Trop J Pharm Res, 2008; 7(3): 1055-1066.
14. Deshpande AA, Rhodes CT, Shah NH, Malick AW. Controlled-release drug delivery systems for prolonged gastric residence: An overview. Drug Dev Ind Pharmacy, 1996; 22(6): 531-539.
15. Whishead B, Fell JT, Collett JH. Development of gastro retentive dosage from. Eur J Pharm Sci, 1996; 4: 182-186.
16. Venkata SM, Ambedkar SS, Sreenivasa RN, Janaki RB, Latha K, Venkata RMK. Thermal sintering: a novel technique in the design of gastro retentive floating tablets of proprannlol HCl and its evaluation. Invest Clin, 2012; 53(3): 223-236.
17. Mohanty C, Subrahmanyam KV, Abdul SM, Jena TK. Thermal sintering technique: a novel strategy used in the design of gastroretensive floating matrix tablets niardipine HCl and its evaluation. Int J Pharm Res Health Sci, 2016; 94(1): 1004-1009.
18. Mohanty C, Subrahmanyam KV, Jena TK, Sreekanth D. Use of sintering technique to sustain the release of atazanavir sulphate from gastro retentive floating matrix tablets. Am J PharmaTech Res, 2015; 5(4): 2249-3387.
19. Srikanth MV, Sunil SA, Rao NS, Ram BJ, Murthy KVR. Thermal sintering: A novel technique used in the design of gastro retentive floating tablets of propranlol HCl and its statistical optimization using box –behnken design. Farmacia, 2012; 60(3): 411-434.
20. Airemwen CO, Uhumwangho MU. Formulation and evaluation of Gastro retentive floating matrix tablets of Metronidazole using a novel non-effervescent technique. Saudi J Med Pharm Sci, 2018; 4(2): 257-264.
21. Seshagiri B, Chowdary KA, Priya YD. Formulation and evaluation of sintered gastro retentive tablets of glipizide. Int J Pharmacy Pharm Sci, 2011; 3(1): 128-135.

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