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Model based process optimization of nanosuspension preparation via wet stirred media milling

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ABSTRACT

The present study focuses on model based parameter optimization of nanosuspension preparation via wet stirred media milling. Based on experimental data of nanomilling a crystalline organic material, two different approaches for process optimization were evaluated: The stress model for stirred media mills, introduced by Kwade, was compared to the microhydrodynamic approach modified by Bilgili and Afolabi. The different approaches to describe influences of operating parameters were discussed with respect to their applicability on process optimization of nanosuspension preparation. Both approaches yield characteristic values which are derived from proportionalities to process parameters. Despite of different physical assumptions, the milling process can be optimized by both approaches. A more detailed insight into physical interactions can be only generated by numerical procedures. Limitations of the applied procedures were observed especially with respect to the accessibility of parameters required for calculation.

1. Introduction

The preparation of nanosuspensions via wet stirred media milling has become an established production technique for different applications. Stirred media milling is a complex process which depends on several process variables, such as mill parameters (stirrer tip speed, grinding media size, type and filling ratio) and suspension properties (solids loading and viscosity), making process development rather difficult. Process development is often focused on reaching a maximum fineness. From the production related point of view, one has to take energy efficiency and production capacity into account, underlining the importance of process optimization.

In general, wet stirred media milling processes are applied to many industries, for example ore liberation in mineral industries, for quality enhancement of ceramics and fillers, for flavor enrichment of food products, as well as in the pharmaceutical industry to enhance pharmacokinetics of active pharmaceutical ingredients and in many other sectors. Despite of all these different products and their special requirements, the physical mechanisms inside the mill are the same. The principle is based on mechanical stress which is transferred to the product particles by colliding and shearing grinding media, leading to particle and/or aggregate fragmentation. This process is influenced by many variables which determine energy efficiency and product quality. There are different approaches to access the most important parameters of stirred media milling in order to characterize and optimize the milling process. Numerical studies of wet operated mills can provide insight into flow characteristics [1–3], as well as grinding media collision frequencies and energies [4–9]. The detailed information which is provided by simulations might be essential for mill design and fundamental scientific investigations, but for accurate calculations a high computational capacity is needed, the required parameters are hardly accessible, and the use of numerical methods is quite elaborate. There is high potential for (online) process optimization using (dynamic) flow sheet modeling, especially for production sites with high throughput capacities [10]. These methods are based on the one hand on material parameters and breakage modeling, e.g. by population balance modeling [11–15], and on the other hand on machine properties, providing information on the stress conditions [16]. Overall the setup of such a simulation sheet needs high work expenditure and is still a focus of research activity. Numerical tools are not yet fully developed and it is rather difficult to apply them for a distinct process optimization task.

More applicable tools for describing the mill performance and process optimization are represented by mechanistic process models. Different approaches for characterizing the mechanisms inside wet operated stirred media mills have been developed. Kwade introduced a stress model to describe the stress intensity *SI* and the stress frequency *SF* of grinding media based on operating parameters of the mill [17]. This approach describes physical mechanisms inside the mill by proportionalities covering the main operating parameters, in order to optimize process efficiency and production capacity [18]. There are

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several studies which have applied the stress model for description and optimization of nanomilling operations of organic particles [19–22].

Another model to describe the grinding media collisions based on the transformation of turbulent flow into kinetic energy of grinding media was introduced by Eskin et al. [23,24]. This approach can be combined with further assumptions regarding particle compression probability and Hertzian contact mechanics in order to calculate the total energy spent on solids deformation. In the end, the so called microhydrodynamic analysis leads to the grinding media size which provides the maximum energy in solids deformation at a certain tip speed for a given product formulation [23]. The model of Eskin et al. was applied with a slight modification to various studies on nanomilling of drug suspensions in order to evaluate the influence of operational parameters and to enhance process intensity [25–28].

The present study focuses on these two approaches and their applicability is discussed based on experimental data. It has to be noted that nanomilling is only possible if the particles are stabilized against agglomeration in order to ensure colloidal stability. The aspect of particle stabilization is not incorporated into these models, all experiments were performed with the same product formulation and differences are discussed with respect to machine parameters.

2. Theoretical

The milling process in stirred media mills is based on grinding media collisions. There are different types, designs and sizes of stirred media mills available on the market but their general operating principle is almost the same. Mechanical power is supplied via the stirrer into the grinding chamber, and the energy has to be transferred finally by the grinding media to the product particles in order to induce particle fragmentation. Process efficiency and production capacity are strongly dependent on operating conditions. In the following, two approaches for the characterization and optimization of stirred media mills are presented and discussed based on the example of milling organic crystalline particles.

2.1. Stress model

Fig. 1 presents a schematic overview of the operating principle of a stirred media mill including the different mechanisms of energy dissipation. Only a small part of the energy which is introduced into the grinding chamber is transferred to the product particles and used for particle stressing [29]. There are different energy dissipation mechanisms which can be classified according to their significance as follows:

A- A high fraction of the energy which is supplied to the grinding chamber is dissipated within the suspension by liquid friction. This mechanism is mainly a function of the suspension viscosity, the applied shear rate, and proportional to the suspension volume fraction inside the grinding chamber. It has to be noted that energy which is transferred to the liquid is not effective for real particle breakage but it may contribute to fluid based dispersion processes.

B- Friction at the grinding chamber wall is determined by geometric aspects, i.e. the surface to volume ratio of the grinding chamber: with increasing mill volume, the proportion of energy dissipated by friction at the wall decreases [30].

C- Suspension is displaced by approaching grinding media, thus kinetic energy is transferred to the fluid. The degree of dissipation depends mainly on the suspension viscosity, and if a critical suspension viscosity was exceeded, real grinding would no longer be possible [31].

D- Grinding media contacts without stressing product particles lead to energy dissipation, this mechanism decreases with increasing solids concentration.

E- Energy dissipation due to grinding media wear and deformation. The degree of deformation is a function of the elasticity ratio between product particles and grinding media, especially product particles with a low elasticity lead to higher dissipation rates due to grinding media deformation [32].

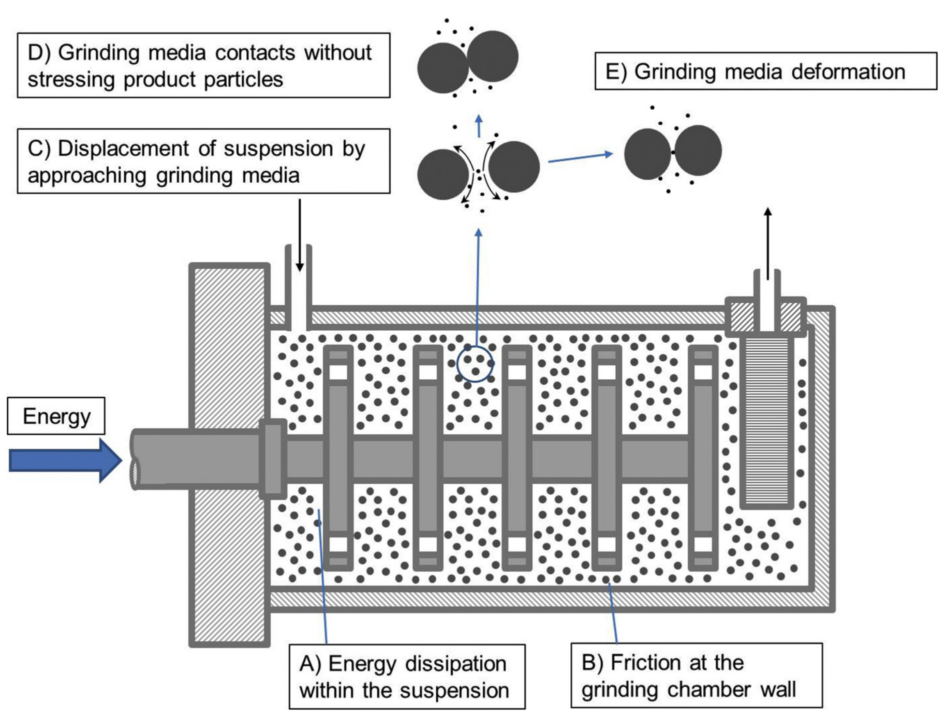

Fig. 1. Schematic overview of the operating principle of a stirred media mill including energy dissipation mechanisms according to Kwade [29].