Usage of compaction simulators for the powder compression characterization – advantages and limitations

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Abstract

Compaction simulators are designed as machines which can provide an in-depth analysis of the powder compaction process. Characterization of the powder compression and compaction process, as well as material characterization, play an important role in the formulation and manufacturing process design and development, as well as in creating a strong knowledge basis for the scale-up of the tablet compression and troubleshooting in further stages of the product lifecycle. Although compaction simulators are designed to simulate the compression process on high-speed tablet-presses, with the advantages of a small quantity of material needed and highly sophisticated instrumentation, there are certain limitations in the extrapolation of the process parameters from these machines to high-speed rotary tablet presses. However, the advantage of the use of compaction simulators for studying basic compression and compaction mechanisms, identification of critical material attributes and critical process parameters ranges, and their relations with tablet characteristics and critical quality attributes of pharmaceutical products is clear, compared to the use of small excentre tablet presses, and complementary to the use of small rotary tablet presses.

This scientific paper provides an overview and examples of the different advantages provided by the instrumentation of compaction simulators, including certain limitations in their exploitation.

Key words: compaction simulator, tablet-press instrumentation, scale-up, compressibility, compression block deformation

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Introduction

Solid oral pharmaceutical dosage forms have been the most commonly prescribed and used therapeutics. Tablets, as one of the most important types among solid oral dosage forms, have been produced by the compression of powders which contain an active pharmaceutical ingredient (API) and excipients. Several types of machines, e.g., tablet presses, are used for powder compression and can be divided in two different categories:

- excentre tablet presses, where die is fixed and the dosing hopper is mobile,
- rotary tablet presses, where the dosing hopper is fixed, and the dies and tooling are mobile.

In excentre tablet presses, it is possible to apply only the lower tableting speed (tablets per hour, tbl./h), due to the limited speed of the moving excentre roller which is moving the hopper and tooling, so they are suitable for the compression of small quantities of powder. Rotary tablet presses are designed for higher tableting speeds and the production of higher quantity of tablets, and are to be used only with a bigger quantity of the powder. Therefore, they are not suitable for the research and development purposes. Due to a smaller quantity of the powder used, excentre tablet presses were predominantly used in research and development with high performance limitations, leading to a high risk for the process scale-up to the high-speed rotary tablet presses. Major differences, which cause difficulties for the scale-up, were different powder behavior and consecutive tablet properties under the higher compression times on excentre tablet presses (> 300 ms) comparing to rotary tablet presses (10 – 30 ms), resulting in tablets with inferior mechanical characteristics prone to capping, lamination, high friability, lower hardness, and different disintegration and consequently dissolution properties. As a result of the need for better material characterization, better evaluation of the powder compression, compaction and tablet consolidation phase, compaction simulators have been developed and used. In compaction simulator, combining the characteristics of single punch station excentre presses, i.e., the use of a small quantity of the product, and short compression times and resulting dwell times of rotary tablet presses, enabled the evaluation of material characteristics under the relevant experimental conditions. Highly sophisticated instrumentation of compaction simulators enabled better characterization of the powder compression and compaction phase, as well as tablet ejection in the tableting process. According to the USP (United States Pharmacopoeia), compression is the reduction in the volume of a powder bed due to the application of stress, e.g., loading, and compaction is the transformation of powder into an intact compact with measurable strength and defined shape by the application of compression pressure.

Tablet formation process

The tableting process on the rotary tablet press can be divided into following phases:

- Dosing of the powder into the die,

- Precompression and main compression,
- Ejection.

The compression of powders into tablets is preceded by the phase of powder dosing into the matrices (dies). Dies, which are positioned on the rotating die table, are filled with powder which is compressed by the mechanical pressure applied through the upper and lower tooling by the use of compression rollers in a corresponding tablet press. As an outcome of the compression phase, a coherent solid tablet, with specific dimensions, weight and shape is formed out of free-flowing powder, and with the movement of the lower punch ejected out of the die and removed from the die table by the action of the scraper (Figure 1).

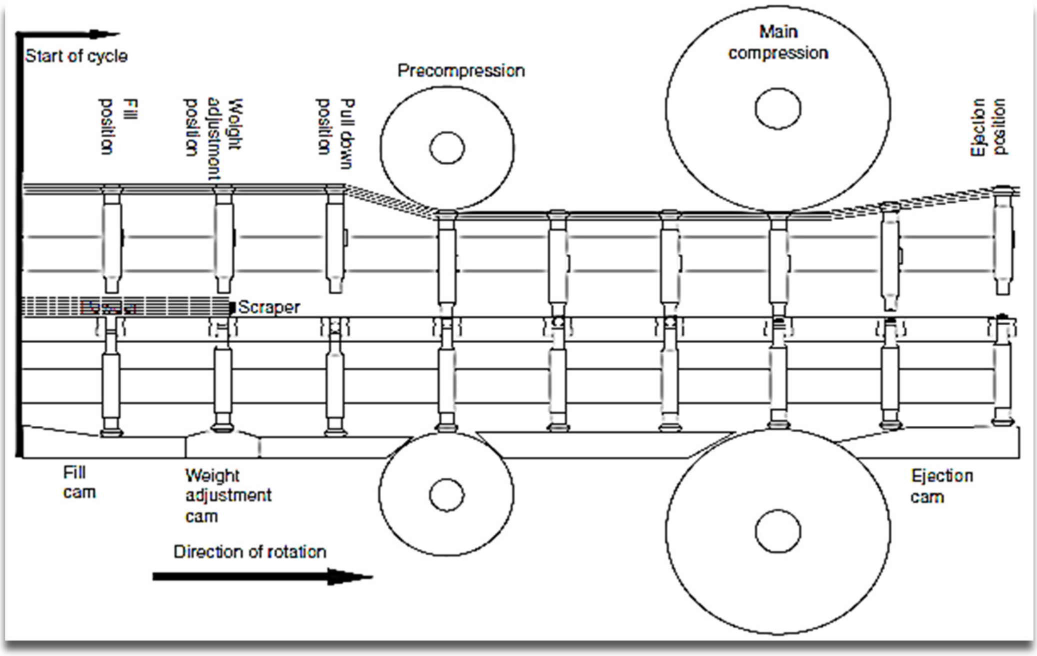

Figure 1. Schematic diagram of the rotary tablet press
Slika 1. Šematski dijagram roptacione mašine za tabletiranje

Considering the tablet formation process according to the diagram above, powder compression after the dosing of the powder into the die can be divided into different subphases (2):

- Deaeration,
- Elastic deformation of particles,
- Plastic deformation of particles,
- Particle fragmentation,
- Forming of the solid bonds,
- Decompression.

The completion of tablet formation is not finished in the die, but after ejection there is elastic relaxation of material which can be detected as radial and axial relaxation of the tablet (3). Extensive elastic relaxation can cause capping and lamination of tablets, as well as film coating cracks (4).

Deaeration of the powder is the initial phase of powder compression, in which the space between the particles is reduced and they are brought in close position. Final deaeration is done with the precompression in which a loose compact is formed. During main compression, the material is subjected to plastic and elastic deformation, including particle fragmentation, in which there are solid bonds formed between particles, and as a result a tablet is formed. The tablet, a solid compact, can be considered a polydisperse system in which the gas phase, i.e., air, is distributed in the continuous solid phase. Following the end of the main compression, decompression of material happens, in which initial relaxation of the compact occurs, after which the tablet is ejected with the lower tooling out of the die. By a combination of materials with different characteristics, and with the use of appropriate process parameters of the compression, a tablet with corresponding critical characteristics can be obtained.

Compaction simulators

The use of the compaction simulator in the development of tablet formulations has been present since the end of the 20th century and has been established as the state of the art in the development of tablet formulation.

Compaction simulators have been designed as a single punch station tableting devices with the possibility to simulate the compaction characteristics of rotary tablet presses. With the single station design, it is possible to use a small quantity of the material, which is fundamental for the research and development purposes. Based on the operating principles of generating compression pressure, there are different types of compaction simulators: hydraulic and mechanical.

Hydraulic compaction simulator

Historically, the first compaction simulator used was a hydraulic one (ESH Compaction Simulator®, Huxley-Bertram). The operating principle of this device includes two closed loop servo-hydraulic actuators, one mounted on the upper and the other below the lower crosshead. The actuators are controlled using the control system with a computer-based virtual control panel software. Hydraulic pressure is applied to the punch heads which are moving towards each other in the tableting die, in which powder is dosed, similarly as in the tablet press. The compaction cycle is pre-programmed from the computer to enable the manufacture of a tablet against a programed compression force profile (5). This device is using the profile of the compression force profile, or the approximative profile of the displacement, in the function of time which is calculated based on the geometric dimensions of the simulated rotary tablet press. Apart from these two operating modes, there are also modes with a constant tooling speed, with the moving of just the upper punch or with both, upper and lower compression punches. The benefits of the use of the hydraulic compaction simulator were presented by Çelik and Marshall. (6). The effect of process variables (tableting speed, force/pressure, etc.) can be determined, as well as compaction mechanisms (elastic/plastic/particle fragmentation), including the scale-up predictions for different tablet presses. However, certain limitations were noticed in the use of these devices for the predictions of the mechanic characteristics of tablets manufactured on rotary tablet presses, although the hydraulic pressure was with the same operating principle at the time. The most obvious one is that there is no possibility to perform the precompression cycle on the machine. Other limitations come from the different machine elasticity of the hydraulic compression simulator and the tablet press, as well as from a lack of possibility to mimic the force and tooling displacement profile relevant for the tablet press which is simulated at the same time. Therefore, the hydraulic compaction simulator served mainly as a research tool for the fundamental characterization of the mechanical behavior of different materials, as well as for studying the different phenomena and tableting problems, lubrication, capping, etc. (7-10).

Mechanical compaction simulators

Apart from the hydraulic type of the compaction simulator, mechanical compaction simulators have been also used. In these machines, compression pressure is generated by the mechanical springs which convey the pressure on the compression rollers, unlike in the hydraulic compaction simulator. Two basic designs have been established:

- Linear replicator of rotary tablet presses, Prester® (MCC, "Metropoliten Computer Company"), in which the tableting tools and die are moving along the linear track, looking like in the diagram of the tablet press presented in Figure 1, and the pressure is transmitted across the compression rollers, same as in the rotary tablet press.
- Compaction simulator with the excentre rotary cam StylCam® and StylOne® (Medelpharm, France), in which the tooling and the die are fixed and are moving only vertically, and compression is transmitted by the excentre rotary cam on the tooling heads. The difference between the StylCam® and StylOne® is that in the StylCam® the pressure on the powder in the die is transmitted by the lower and upper excentre cam, while in the StylOne® only via the lower cam.

It can be seen from the machine design what the limitations for the mimicking rotary tablet press are. Comparing to the hydraulic compaction simulator, the difference is that in mechanical compaction simulators there is a precompression simulation in both types. In the linear replicator, although there is a physically identical model of the moving of the tooling and dies as in the rotary tablet press, a limitation to completely mimicking a certain tablet press is that there is no possibility to simulate different roller diameter in the precompression station as well as in the main compression station, and the distance between the precompression and compression is fixed, and it is not possible for it to be adjusted. By the rotary excentre cam types, different distance, or more precisely, time, between precompression and main compression, can be simulated based on the calculated roller dimension, but limitations regarding pressure transducing to the powder via upper and lower tooling in comparison to rotary tablet presses are present. In the rotary tablet press, transducing of the pressure is done in dependence on the adjusted compression zone, while in the StylCam® and StylOne® the pressure transducing is done either equally with the upper and lower punch on the StylCam®, or only through the lower punch as action and the upper as reaction on the StylOne®, which can cause asymmetric porosity of the lower and upper surface of the resulting tablet. However, regarding the possibility to use the machines for multilayer tablets, as well as for compression coating, this is possible only with the use of the StylOne® compaction simulator. Other types of mechanical simulators or hydraulic compaction simulators cannot be used for these features. The concept of emulation of different rotary tablet presses in the compaction simulator with the excentre rotary cam is based on the simulation of the critical times in the compression cycle in the rotary tablet press: precompression time, precompression/main compression relaxation time, main compression time, main compression/beginning of the ejection time and ejection time. The relevant times are calculated based on the geometric characteristics of the simulated tablet presses (Figure 2) and dimensions of precompression rollers (D2), main compression rollers (D3), and of the die table (D1).

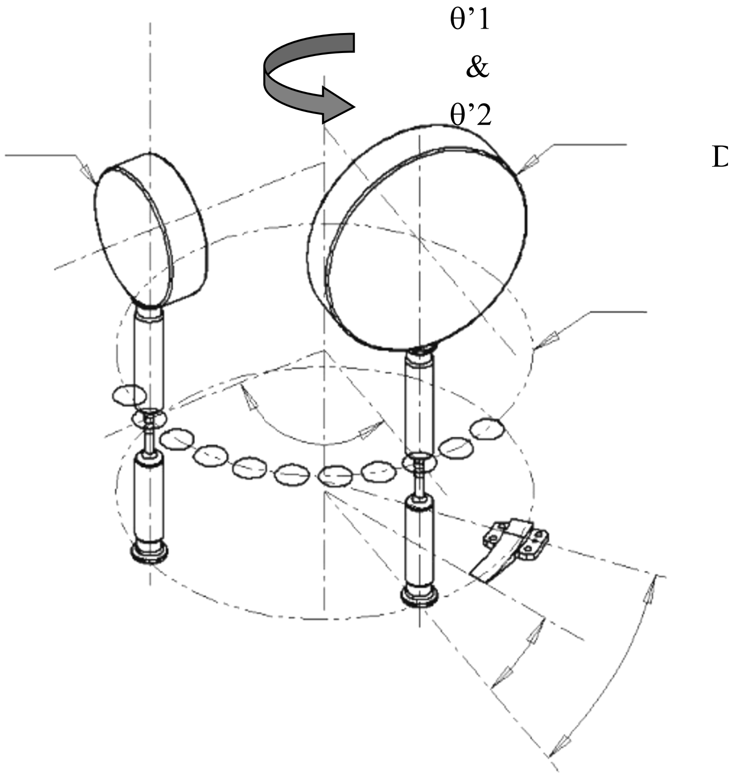

Figure 2. Dimension diagram of the tablet press (11)
Slika 2. Dimenzioni dijagram masine za tabletiranje

Along with the diameter of the rollers and the die table of the referent tablet press, angle distances θ1, θ2 and θ3 are also important for a precise simulation of times for the corresponding tablet press operating on the selected tableting speed in the θ'1-θ'2 range. θ1 is the angle between the axis of the precompression roller and main compression roller, which determines the time between the precompression and main compression in the simulated tableting speed in the θ'1-θ'2 range. θ2 is the angle between the axis of the main compression roller and the ejection cam, which determines the time between the main compression and ejection in the simulated tableting speed in the θ'1-θ'2 range. θ3 angle represents the length of the ejection cam and determines the time of ejection in the simulated tableting speed in the θ'1-θ'2 range of the referent rotary tablet press. In a similar way to the hydraulic compaction simulator, in the mechanical compaction simulator basic limitations are in the focus on the time emulations, but not emulations of the compression force vs time distribution and punch displacement vs time emulation of the referent rotary tablet press.

Compaction simulator instrumentation and corresponding functions

The possibility for powder compression and compaction characterization by the use of compaction simulators comes from the improved instrumentation in comparison to the conventional rotary tablet presses (12). In a similar way to rotary tablet presses, compression forces are monitored, as well as punch displacement (13). The instrumentation in compaction simulators is significantly improved, enabling more precise measurement, more developed positions for the force monitoring, and a much higher frequency of the sampling rate. Usually, there is only precompression and main compression force monitoring on rotary tablet presses, and in special cases ejection force monitoring (research and development small rotary tablet presses). Data sampling frequency rate in rotary tablet presses is usually in the 500-1000 Hz range, which significantly limits the quality of compression profile modeling, as well as the ejection profile. Usually, compression times in the rotary tablet press is in the range of 5–30 ms, predominantly below 15 ms for high-speed rotary tablet presses, which limits the number of points for compression profile cycle modeling to 5–15 points, which in turn increases the probability of the error, and the ejection phase is monitored with very few measurements, which makes the ejection profile characterization almost impossible. However, the sampling frequency in compaction simulators is usually in the range of 2000–20000 Hz, which significantly improves the compression and ejection profile characterization precision.

Compression and ejection profiles

Analyses usually include compression force profiles vs time including displacement profiles (Figure 3).

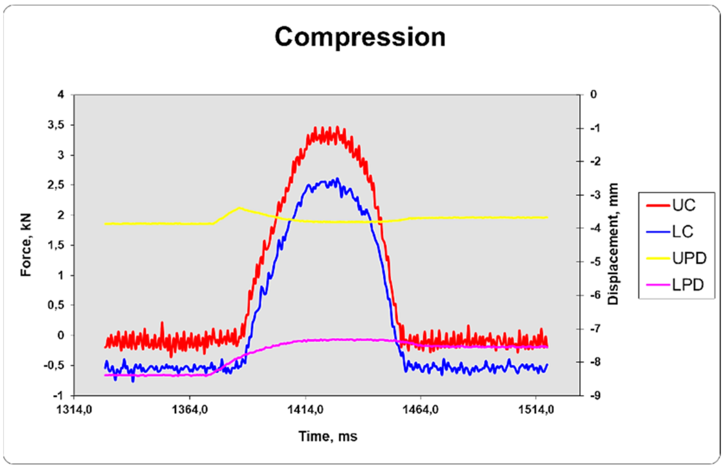

Figure 3. Compression force and displacement profile, MCC Pressster® (14)
Slika 3. Profil sile kompresije i distance, MCC Prester® (14)

In the graph (14), upper compression force (UC) and lower compression force (LC) distribution vs time, as well as upper and lower punch displacements (UPD and LPD) can be identified. An example of the complete precompression/main compression/ejection cycle is presented in Figure 4.

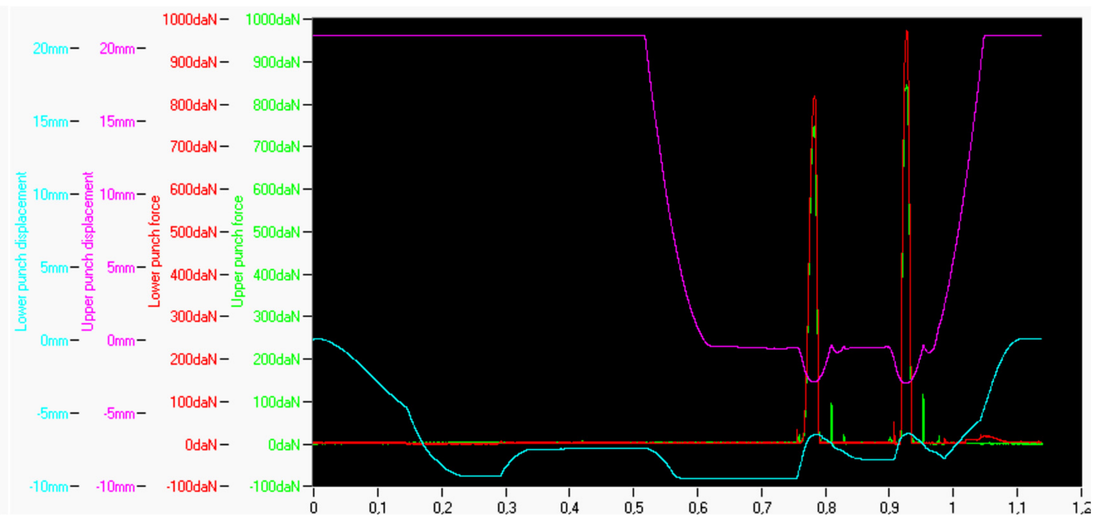

Figure 4. Precompression/main compression/ejection cycle, StylCam 200R®(11)
Slika 4. Ciklus pretkompresije / glavne kompresije / izbijanja, StylCam200R®(11)

The picture shows the movement and displacement of the upper and lower punch during the precompression, main compression and ejection, as well as the force distribution over time. Peaks of the forces show the maximum precompression, main compression force, as well as the peak of the ejection force. Comparing the ejection characterization on the linear mechanical compaction simulator (Figure 5) and compaction simulator with excentre rotary cam (Figure 4), it can be seen that the ejection in the compaction simulator with excentre rotary cam shows the pure ejection force, i.e., the force applied by the lower punch tooling to eject tablet from the die. On the other hand, during the measurement of the ejection force in MCC Presster®, the collision of the lower punch with the ejection cam is also measured, and especially with a high tableting speed, the simulation hinders the ejection force used for the tablet ejection from the die.

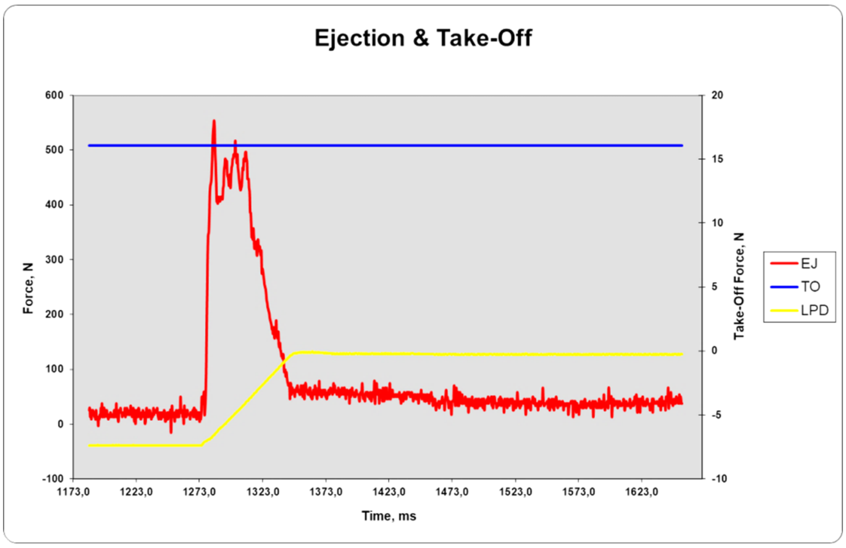

Figure 5. Ejection and tablet take-off profile, MCC Presster® (14)
Slika 5. Profile izbijanja i skidanja tablete, MCC Presster® (14)

The following critical process and compression cycle parameters can be derived from the diagrams and calculated by use of machine algorithms:

- maximal upper and lower compression force,
- maximal upper and lower precompression force,
- contact times (precompression and main compression),
- dwell times during precompression and main compression, time at the start and half of dwell time,
- minimal and maximal punch displacement,
- time to achieve minimal distance,
- relaxation time,
- minimum in-die volume,
- maximal tablet density,
- porosity functions (vs time, vs force),
- ejection force and time,
- area under the curve for the compression and decompression,
- slopes of the ascendent and descendent force curves,

and many other parameters, which could be important for the compression characterization. The utilization of the compression and ejection profiles has been used for investigation of different compression and ejection phenomena, such as the occurrence of capping and lamination due to ejection (15), effect of the tableting speed prediction on the porosity and tensile strength of the resulting tablets (16), as well for getting information about powder compressibility and tensile strengths of the compacted tablets (17–19). Displacement measurements are limited with the rotary tablet press, as readings of adjustments of different step motors are usually used, and exact displacement measurements are usually not performed. The avoidance of exact readings of the displacement in rotary tablet presses and the use of the step motor position readings is very limiting, especially using it in the compression profiles characterization, because it makes an approximation in the position reading and does not take into consideration effect of the "deformation of the compression block".

Force-displacement profiles

Force-displacement figures (Figure 6) can also be derived from the sampling of the signal from the referent force and displacement sensors (upper or lower force and the corresponding displacement).

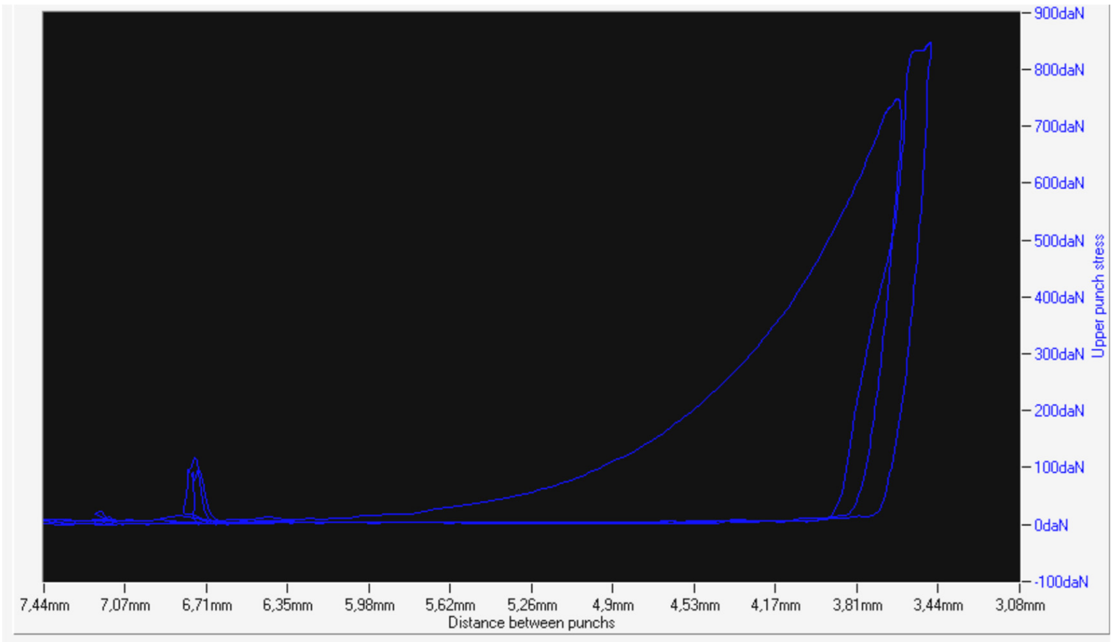

Figure 6. Force displacement diagram, StylCam 200R® (11)
Slika 6. Dijagram sile i distance , StylCam 200R® (11)

With the use of the force displacement diagram, different material deformation characteristics, as well as compression energies during the compression cycle, can be analyzed:

- energy given to the tablet when the force increases,
- elastic energy: energy recovered from the tablet when the force decreases (E_F),
- plastic energy: total energy given to the tablet (E_P),
- ejection energy: energy given to the tablet to be removed out of the die (E_E).

As presented in Figure 7, different functional relations between the force and displacement (i.e., distances between punches) during the compression cycle, as well as energy effects, can be analyzed.

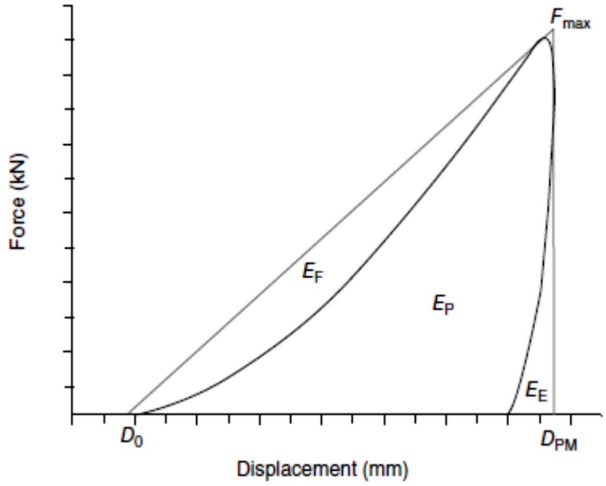

Figure 7. Force displacement figure and corresponding energies during the compression cycle (20)

Slika 7. Grafik sile i distance i odgovarajućih energija tokom ciklusa kompresije (20)

In the force-displacement diagram based on the compression and decompression areas, the energy of interparticle friction can be estimated (E_F), as well as the extent of the plastic and elastic deformation which can be used for the calculation of the porosity functions (6) and porosity of the resulting tablet, as well as for the estimation of the capping and lamination potential (16).

Pressure-porosity functions

Compaction simulators can perform Heckel analysis, which assists in characterizing the deformation behavior of materials using a simulator, which gives a better understanding of pharmaceutical materials. The Heckel function is applied to the pressure-porosity relationship during the compression, or to establish functional dependency between the applied pressure and porosity of the tablets, resulting from different compression pressure (20). The obtained diagram can be evaluated as an in-die porosity if the graph is evaluated from the calculation of the volume of the powder during one compression cycle, or out-die porosity if the porosity is determined from the volume of the resulting tablets with the use of different compression pressures (Figure 8).

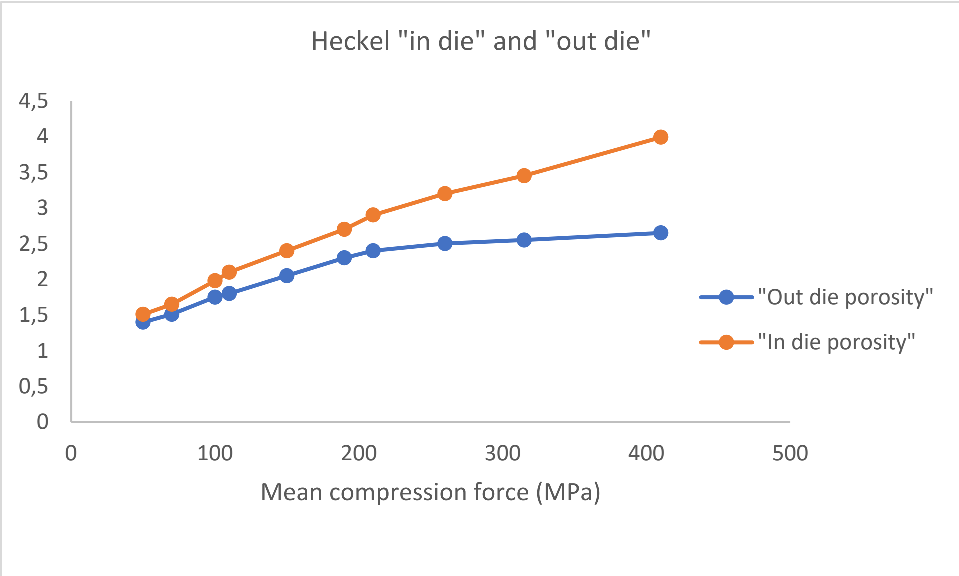

Figure 8. In-die vs out-die porosity graph (11)
Slika 8. Grafik poroznosti unutar-matrice vs. van-matrice (11)

Pressure-porosity functions have been used for material characterization, i.e., their compressibility (22-24) or determination of the mechanism of the material deformation (elastic vs plastic or fragmentation (25)). The importance of establishing the relation of three powder characteristics: compressibility, compactibility and tabletability, has been highlighted by the Amidon (26).

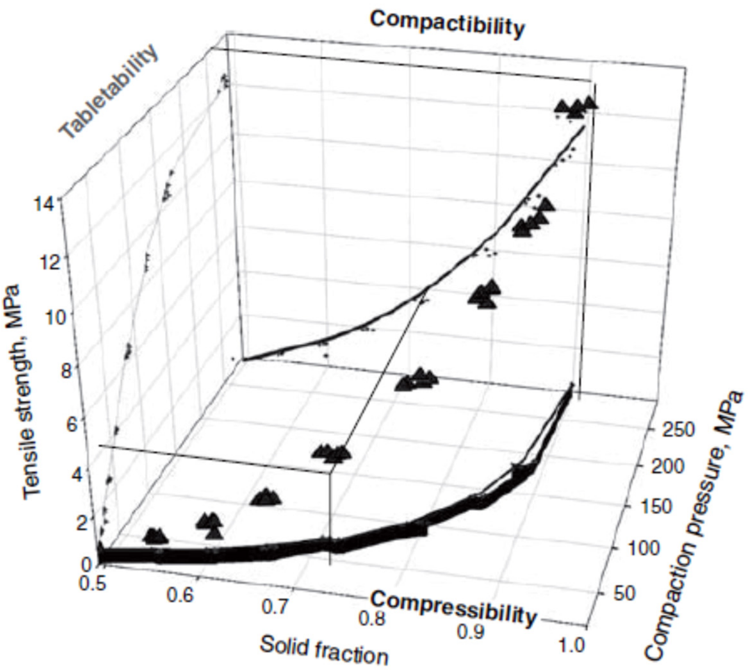

Figure 9. Compressibility, compactibility, tabletability profile (26)
Slika 9. Profil kompresibilnosti, kompatkibilnosti i tabletabilnosti (26)

By establishing these material characteristics profiles, it was possible to establish the desirable design space of the tablet formulation and critical process parameters of the tableting process. A prediction of the dissolution profiles of matrix tablets based on the tablet porosity, taking into consideration compactibility and tabletability, was also done by Nikolic (14).

Other measurements

Compaction simulators also have a possibility of radial wall pressure measurements in the die. Only recently has a method for the measurement of radial die wall pressure in the rotary tablet presses been developed (27). The measurement of the radial wall pressure enables the evaluation of the influence of different factors on the lamination and capping occurrence caused by high radial wall pressure. There have also been different studies of the influence of different punch geometry (28) on the radial die wall pressure, and in-die friction which can cause mechanical problems with tablets. As already presented earlier, it is possible to measure the take-off force to evaluate the force necessary to remove the tablet from the lower punch face and to identify the sticking tendency during tableting.

Scale-up studies

Compaction simulators can be used for establishing emulations of different rotary tablet presses. As previously described, certain limitations have been identified in different simulator types: lack of precompression simulation in hydraulic compactors, lack of precompression to main compression relaxation time, as well as main compression to ejection time in the linear mechanical compaction simulator, and use of both compression profile simulation and displacement profile simulation. The measurement of the displacement errors on rotary tablet presses has also induced further difficulties to emulate displacement and relevant compression profiles. However, there have been extensive studies of the correlation and prediction of tablet characteristics manufactured on high-speed rotary tablet presses by the use of established emulation of the specific model of the rotary tablet press in compaction simulators (29-31). To be able to use the relevant experimental field as much as possible, compaction simulator with the excentre rotary cam has been utilized to simulate times of the precompression, main compression and ejection, including times between the precompression and main compression and main compression and ejection. Additionally, the deformation of the compression block model is also included in the measurements to distinguish between the real and calculated dwell times, which enables determination of the real dwell times during the compression. As dwell time is considered critical for the evaluation of useful compression work, it is essential for a successful scale-up to have a relevant estimation of the dwell time and energy calculations, taking into consideration all mechanical deformations during the compression. Deformation of the compression block represents a correction of the displacement, which occurs with different speed and different force for the used tablet compression machine. This practically means that the displacement measured under different pressure or stress has to be corrected in the calculation of dwell time, i.e., time in which the corresponding distance between the tooling punch faces is minimal and constant, and compression force increase provides compression work in the formation of the compacted powder, i.e., tablet. In the compression profile figure (Figure 4), this corresponds to the intercept of displacement line in the graph and the compression force line. In the case of MCC Pressster® (Figure 3), there is no correction for the compression block deformation; therefore, it is not possible to distinguish between the calculated and real dwell time. The corresponding deformation is constructed for the machine with the use of different speed of the rotating cam and range of the compression forces (Figure 10).

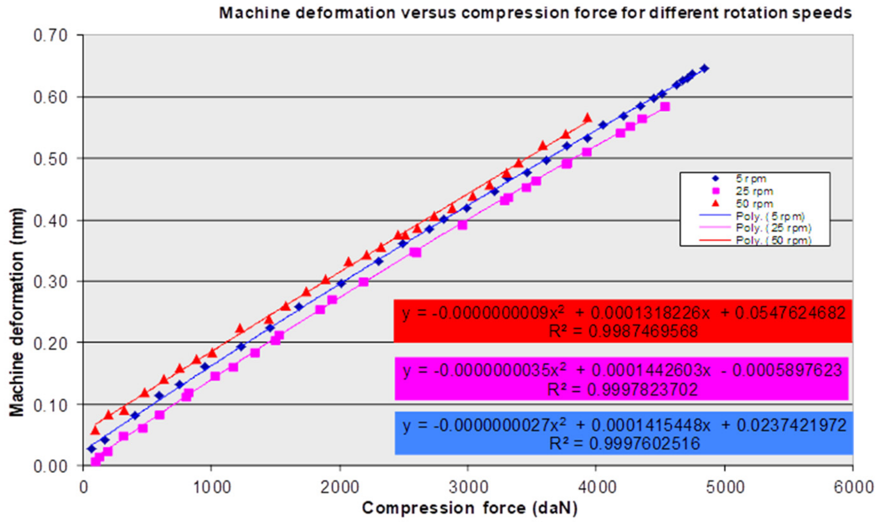

Figure 10. Deformation of the compression block with the minimal, middle and maximal rotating cam speed (11)

Slika 10. Deformacija kompresionog bloka na minimalnoj, srednjoj i maksimalnoj brzini bregaste osovine (11)

As the outcome of the deformation of the compression block, corresponding quadratic models are established, which are used for the conversion of theoretical dwell time into real dwell time. In practice, corrected dwell times are always shorter than theoretical, as presented in the table below, which represents a calculation of the corrected times, taking into consideration machine deformation done by the Analys software of the compaction simulator StylCam200R during the execution of one compression cycle (11).

Table I Example of real dwell time vs theoretical dwell time (11)

Tabela I Primer poređenja realnog i teoretskog vremena zadržavanja alata (11)

Machine Speed (Simulated machine - Simulated machine speed) : 25 RPM (Direct cam - N/A)					
	Average	**Min**	**Max**	**Max-Min**	**Srel**
Die filling height (mm)	18,430	18,429	18,432	0,003	0,00
Upper punch pre-compression force (daN)	252	241	265	24	2,37
Lower punch pre-compression force (daN)	250	238	264	26	2,41
Upper punch pre-compression displacement (mm)	2,590	2,586	2,593	0,007	0,07
Lower punch pre-compression displacement (mm)	7,508	7,503	7,513	0,010	0,04
Pre-compression thickness (mm)	4,918	4,913	4,923	0,011	0,06
Corrected pre-compression thickness (mm)	4,970	4,965	4,975	0,010	0,06
Theoretical pre-compression time (ms)	183	181	184	3	0,41
Real pre-compression time (ms)	19	19	21	2	3,63
Real pre-compression dwell-time (ms)	7	6	7	1	3,33
Theoretical pre-compression dwell-time (ms)	21	21	22	1	1,12
Theoretical relax time (ms)	137	136	138	1	0,31
Relax time (ms)	296	295	297	2	0,20
Upper punch compression force (daN)	530	519	539	20	1,08
Lower punch compression force (daN)	524	512	533	22	1,24
Upper punch compression displacement (mm)	2,663	2,659	2,665	0,006	0,06
Lower punch compression displacement (mm)	7,542	7,535	7,548	0,013	0,04
Compression thickness (mm)	4,880	4,874	4,884	0,010	0,07
Corrected compression thickness (mm)	4,970	4,963	4,973	0,010	0,06
Theoretical compression time (ms)	177	176	178	2	0,37
Real compression time (ms)	21	21	21	0	1,20
Real dwell-time (ms)	7	7	7	1	3,59
Theoretical dwell-time (ms)	22	22	23	1	0,97
Theoretical relax time before ejection (ms)	56	48	60	12	4,95
Real relax time before ejection (ms)	131	123	135	12	2,10
Ejection force (N)	147	105	178	74	14,15
Ejection time (ms)	88	83	96	13	3,11
Take-off maximum force (N)	0,3	0,3	0,4	0,0	0,37
Rearrangement Energy (J)	35,570	34,818	36,209	1,391	1,15
Compression Energy (J)	-0,107	-0,140	-0,058	0,081	-17,65
Flow Energy (J)	0,002	0,000	0,006	0,006	89,30
Elastic Energy (J)	-0,032	-0,042	-0,019	0,023	-21,24
Plastic Energy (J)	-0,139	-0,168	-0,094	0,074	-12,82
Ejection Energy (J)	1,061	0,811	1,287	0,476	13,99

This correction explains uncertainties between the emulation model in the compaction simulator and in the real rotary tablet press, since the deformation of the compression blocks of the tablet press is usually not taken into consideration, but only the geometrical characteristics. However, this approximation is also the root cause of the different behavior of the two tablet presses of the same model, as well as of the two different compression stations in the same tablet press. Other examples in the praxis are the change from the tableting with the single tip tooling to the multi-tip tooling, as well as the change of the tooling material with different elastic and plastic behavior. To be able to distinguish and to extrapolate data, it is necessary to take the characteristics of the compression block into consideration under different tableting speed and different compression force.

Conclusion

Compaction simulators are the state of the art in tablet formulation development, as well in scale-up of the tableting process, transfer to the production and troubleshooting in the routine production. Appropriate use of compaction simulator data is necessary to be able to adequately extrapolate data from studies to large-scale production tablet presses. Although compaction simulators provide many possibilities for the material characterization and compression and compaction evaluation, it is necessary to apply numerous approximations for establishing the reliable experimental area and design space.

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Upotreba simulatora kompaktiranja za karakterizaciju kompresije praškova – prednosti i ograničenja

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Kratak sadržaj

Simulatori kompaktiranja su uređaji dizajnirani da omoguće dublju analizu procesa komprimovanja praškova. Karakterizacija procesa kompresije i kompakcije praškova, kao i karakterizacija materijala, ima važnu ulogu u dizajnu i razvoju formulacije i proizvodnog procesa tableta, kao i za kreiranje snažne baze za transfer proizvodnog procesa komprimovanja tableta na proizvodnu opremu i rešavanje problema u proizvodnim procesima u kasnijim fazama životnog ciklusa proizvoda. Iako su simulatori kompaktiranja dizajnirani da simuliraju proces kompresije na tablet-presama visoke brzine, obezbeđujući prednost korišćenja manjih količina materijala i visoko sofisticirane instrumentacije, postoje određena ograničenja u ekstrapolaciji procesnih parametara sa ovih mašina na tablet-prese visokih brzina. Međutim, prednosti upotrebe simulatora kompaktiranja za proučavanje osnovnih mehanizama kompresije i kompaktiranja, identifikaciju kritičnih karakteristika materijala i opsega kritičnih procesnih parametara, kao i njihovih relacija sa karakteristikama tableta, i kritičnim karakteristikama farmaceutskih proizvoda su očigledne, u poređenju sa korišćenjem malih ekscenter tablet presa, i komplementarne sa upotrebom manjih rotacionih tablet presa. U ovom radu je prikazan pregled i primeri različitih prednosti omogućenih nivoom instrumentacije simulatora kompaktiranja, uključujući i ograničenja u njihovoj eksploataciji.

Ključne reči: simulator kompaktiranja, komprimovanje praškova, instrumentacija tablet-presa, kritični procesni parametri, kompresibilnost

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