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RESEARCH

Study of Co-processed Excipient for Direct Compression Using the SeDeM-ODT Expert System

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Abstract

Background This study aimed to identify suitable excipients for the development of vitamin C orally disintegrating tablets (ODTs) using the SeDeM-ODT expert system as a systematic preformulation tool for direct compression.

Methods Vitamin C and seven excipients, including both co-processed materials (Prosolv® ODT G2, Parteck® ODT, Ludiflash®, and Ludipress® LCE) and single-component excipients (EMDEX®, Ceolus™ UF-702, and Ceolus™ UF-711), were evaluated based on SeDeM-ODT parameters related to powder flowability, compressibility, lubricity/stability, lubricity/dosage, and disintegrability. The suitability of each material for direct compression was assessed using the Index of Good Compressibility and Bucodispersibility (IGCB).

Results Vitamin C alone exhibited poor compressibility, flowability, and disintegrability, resulting in an IGCB value below the acceptable limit and confirming its unsuitability for direct compression ODT formulation. Among the investigated excipients, Ludiflash®, Parteck® ODT, and Ceolus™ UF-702 achieved IGCB values above the acceptance threshold and were therefore selected for tablet formulation studies. Tablets prepared with these excipients (100 mg vitamin C, 200 mg excipient, and 1% magnesium stearate) were produced by direct compression and evaluated for mechanical strength, friability, disintegration time, and dissolution performance. All formulations exhibited acceptable tablet characteristics, including uniform weight, adequate mechanical strength, and rapid disintegration within pharmacopeial limits for ODTs. Dissolution testing confirmed rapid drug release, with more than 75% of vitamin C released within 45 min, and early-stage release occurring within the first minutes after disintegration.

Conclusion Overall, the results demonstrate that the SeDeM-ODT expert system provides a reliable framework for excipient selection in ODT development, and confirm that Ludiflash®, Parteck® ODT, and Ceolus™ UF-702 are suitable excipients for the preparation of vitamin C orally disintegrating tablets by direct compression.

Keywords Orally disintegrating tablets · SeDeM-ODT expert system · Co-processed excipients · Direct compression · Disintegration

Introduction

Orally disintegrating tablets (ODTs) are solid oral dosage forms designed to disintegrate or disperse rapidly in the oral cavity (typically within seconds), forming a dispersion that is swallowed, which can facilitate subsequent drug dissolution and improve patient acceptability and adherence. To achieve fast disintegration, the formulated tablet must ensure high porosity, low density, and low tablet breaking force [1]. Over the past decade, there has been a substantial increase in the demand for the development of ODTs, significantly impacting patient compliance [2]. Particularly beneficial for those with difficulty swallowing, ODTs address the common issue of dysphagia across age

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groups, notably in the pediatric and geriatric population [3, 4]. Despite the advantages of orally disintegrating tablets for pediatric and geriatric populations, the palatability of the dosage form remains a major formulation challenge. Referred to by various names such as orodispersible tablets, quick disintegrating tablets, mouth dissolving tablets, fast disintegrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets, and rapid melts [5, 6]. The United States Pharmacopoeia (USP) officially recognizes them as orally disintegrating tablets, with the FDA defining ODT as ''A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly, usually within a matter of seconds when placed upon the tongue'' [7]. The European Pharmacopoeia terms them "Orodispersible tablets" if they disperse readily in the mouth within 3 min before swallowing [8].

Multiple methods are available for manufacturing ODTs, including molding, lyophilization, freeze-drying, and direct compression. There are other methods available, such as cotton candy and spray drying [9, 10]. While lyophilization and spray drying were previously common methods with low disintegration time, conversely, low mechanical strength [11, 12]. Special packing was required for ODTs prepared by these techniques, and they were highly fragile. Additionally, these methods necessitated specialized equipment and were unsuitable for large doses of water-insoluble drugs [13]. Direct compression is now widely used. However, optimization of powder blend characteristics remains a challenge in direct compression. For the direct compression method to meet official requirements, the powder blend must possess optimum powder flow properties, mechanical strength, and disintegration behavior [14].

Co-processed excipients are attracting attention as they enhance functionality by combining the properties of individual excipients into a single particle. Produced through physical processing without chemical modification, they usually require less extensive toxicological evaluation [15]. By combining the favorable properties of individual excipients, co-processed excipients tend to be effective physical mixtures in pharmaceutical properties [16, 17]. Previous research has reported that combining excipients by co-processing can enhance content uniformity and reduce segregation problems in dosage units [16]. A co-processed excipient is used to support tablet manufacturing through the direct compression method. Despite their well-recognized technological advantages, the use of co-processed excipients in pharmaceutical formulations may present regulatory and registration challenges [15].

In the past, the development of pharmaceutical formulations relied mainly on experiments and research experience, which were slow and expensive processes. However, the SeDeM expert system, developed by Carreras et al. [18], has the potential to streamline this process by implementing the concept of pharmaceutical quality by design (QbD). QbD is a systematic approach that employs quality risk management and sound scientific principles to create new pharmaceutical products [19]. This is a new galenic method that is used in tablet pre-formulation and formulation studies, particularly for the DC method. Evaluating the powder characteristics of active pharmaceutical ingredients (APIs) and excipients by using the SeDeM diagram to determine their suitability for DC manufacturing or the need for additional excipients. Lately, the SeDeM-ODT expert system, an advancement, includes a Disgregability factor, enhancing the assessment of excipient properties [20].

This study aimed to predict suitable developed co-processed excipients using the SeDeM-ODT expert system to obtain orally disintegrating tablets for Vitamin C by the direct compression method. Although the SeDeM-ODT expert system and the investigated excipients are not novel individually, the originality of this work lies in their integrated and comparative application to a mechanically challenging API. By systematically evaluating excipients from different functional classes within a single SeDeM-ODT framework and validating the screening outcomes with tablet-level performance data, this study provides a decision-oriented approach to excipient selection for direct compression ODT development.

Materials and Methods

Materials

Vitamin C (ascorbic acid) was received as a gift from HL Vitamin (Luwei Pharmaceutical Group Co., Ltd., China). The co-processed excipients for DC tablets were generously obtained as gifts from suppliers, including Prosolv® ODT G2 and Emdex® (JRS Pharma, USA), Ceolus™ UF-702 and Ceolus™ UF-711 (Asahi Kasei Chemicals Co., Japan), Parteck® ODT (Merck, Germany), Ludiflash® and Ludipress® LCE (BASF, Germany). Magnesium stearate was also received as a gift from Faci (Faci Asia Pacific Pte Ltd, Singapore). All other chemicals were analytical grade.

Methods

Characterization of Powders

Characterization of Vitamin C was evaluated based on the SeDeM-ODT expert system. The co-processed excipients were performed using the SeDeM-ODT expert system. Some basic parameters according to SeDeM-ODT were

experimentally performed, which were repeated in triplicate, while others were calculated relying on the values of basic parameters [20, 21], as presented in Table S1. The following are the details for determining parameters:

Dimension

Bulk Density: According to Method I of the United States Pharmacopeia (USP) < 616>, bulk density and tapped density of powders were determined [22].

Tapped Density: According to Method I of the USP < 616>, bulk density and tapped density of powders were determined [22].

Compressibility

Inter-Particle Porosity: According to tapped density and bulk density values, it was calculated using the equation specified in Table S1.

Carr's Index: According to the USP < 616>, bulk density and tapped density of powders test [22], tapped density and bulk density values were used to calculate Carr's Index based on the equation specified in Table S1.

Cohesion Index: According to the Aguilar-Díaz et al. study [23], it was determined by compressing the raw powder with convex face punches and a 6 mm diameter. The compression force was 500 psi unidirectional. Then, the average breaking force (N) of the tablets (n = 3) was measured.

Flowability/Powder flow

Hausner Ratio: According to the USP < 616>, bulk density and tapped density of powders test [22], tapped density and bulk density values were used to calculate Hausner Ratio based on the equation specified in Table S1.

Angle of Repose: The angle of repose was determined using the funnel method, according to < 1174>, powder flow test instructions [24]. Measured the amount of powder placed in a funnel that was fitted at a specific height (3.5 cm) from the tabletop and allowed the powder to pass through the funnel's orifice. Measurement of the radius and height of the powder cone was used to calculate the angle of repose using the equation from Table S1. Determination was carried out in triplicate, and then the mean value was calculated.

Powder Flow: Powder flow was determined using the method prescribed by the USP < 1174>, powder flow test instructions [24]. Measured the amount of powder placed in a funnel and then allowed the powder to pass through the funnel's orifice. The time it took for the powder to flow was recorded.

Loss on Drying: The loss on drying was determined using the method in accordance with USP's < 731 > instructions [25]. The sample (1 g) was heated in the Nuve EN 055 Incubator (Nüve, Turkey) at 100 °C until a constant weight was achieved, then the weight loss percentage was calculated. Determination was carried out in triplicate, and then the mean value was calculated.

Hygroscopicity: The hygroscopicity was evaluated by measuring the mass increase of the powder under controlled humidity conditions (75 ± 5%) for 24 h, and the percentage mass gain was used as a quantitative indicator of hygroscopicity [26].

Particle size (%Pf): The proportion of particles passing through a 50 µm sieve was determined by sieve analysis. A vibratory sieve shaker (Vibro, Retsch, Germany) was operated at an acceleration of 1 g for 10 min [27].

Homogeneity Index: To define the homogeneity index of the powder, Aguilar-Díaz et al. and Suñé-Negre et al. studies were used [26, 28]. A sieve vibrator (Vibused, Retsch, Germany) was used, and sieves were placed in decreasing order based on particle size (710, 500, 300, 212, 125, 90, 75, and 50 µm). A sieve vibrator (Vibro, Retsch, Germany) shook for 10 min at a speed of 10. The amount of powder retained over each sieve and that which passed through the 50 µm sieve was determined by a percentage based on the following Eq. 1.

$$
\begin{aligned}
*I\theta = {} & \mathrm{Fm}/100 + (\mathrm{dm} - \mathrm{dm} - 1)\,\mathrm{Fm} - 1 \\
& + (\mathrm{dm} + 1 - \mathrm{dm})\,\mathrm{Fm} + 1 + (\mathrm{dm} - \mathrm{dm} - 2)\,\mathrm{Fm} \\
& -2 + (\mathrm{dm} + 2 - \mathrm{dm})\,\mathrm{Fm} + 2 + \ldots.. \\
& + (\mathrm{dm} - \mathrm{dm} - \mathrm{n})\,\mathrm{Fm} - \mathrm{n} + (\mathrm{dm} + \mathrm{n} - \mathrm{dm})\,\mathrm{Fm} + \mathrm{n}
\end{aligned}
\tag{1}
$$

Effervescence Time: The effervescence time was determined following the USP [29] guidelines. Firstly, tablets were prepared by applying maximum compression force until capping and lamination occurred. Next, a beaker was filled with 200 mL of distilled water, and a tablet was added to it. The time it took for the compact to completely disperse was noted. Determination was carried out in triplicate, and then the mean value was calculated.

Disintegration Time with Disk: Tablets were prepared by applying maximum compression force until capping and lamination occurred, and then the tablet underwent a test to determine its disintegration time while a disk was present, following the guidelines set by the USP [29]. Distilled water was the disintegration medium. Determination was carried out in triplicate, and then the mean value was calculated.

Disintegration Time without Disk: Tablets were prepared by applying maximum compression force until capping and lamination occurred, and then the tablet underwent a test to determine its disintegration time while a disk was absent, following the guidelines set by the USP [29]. Distilled water was the disintegration medium. Determination was carried out in triplicate, and then the mean value was calculated.

Conversion of Experimental Values (V) to Radius Values (r) and Determination Index of Good Compressibility and Bucodispersibility (IGCB)

Table S1 presents a summary of the basic parameters of the SeDeM-ODT expert system, along with their formulas, and the essential factor used to convert experimental values (V) to radius values (r). Then the results are presented graphically. After collecting the necessary data, a SeDeM-ODT diagram was created, which included 15 polygons for each parameter. The radius scale for the diagram ranged from 0 to 10, and the minimum acceptable value for each parameter was set at 5. The parameters were then combined into six incidence factors [21, 23, 30].

A set of indices was calculated to determine the quality attributes of a powder. These indices include the Index Parameter (IP), Index Profile Parameter (IPP), and Index of Good Compressibility and Bucodispersibility (IGCB).

The Parametric Index (IP) is the proportion of parameters that have (r) values equal to or greater than 5 to the total number of parameters found during the analysis. Acceptable value is equal to or higher than 0.5. Equation 2 used to calculate the IP is as follows:

$$\mathrm{IP} = \mathrm{No.P} \geq 5/\mathrm{No.Pt} \tag{2}$$

Parameter Profile Index (IPP) is the mean value of (r) values for all parameters, as seen in Eq. 3. The minimum acceptable value of IPP is 5.

$$\mathrm{IPP} = \text{Mean radius values of all parameters} \tag{3}$$

Good Compressibility and Bucodispersibility Index (IGCB) is determined by multiplying IPP with a reliability factor. To calculate the IGCB, Eq. 4 was used.

$$\mathrm{IGCB} = \mathrm{IPP} \times \mathrm{f} \tag{4}$$

In Eq. (4), the symbol (f) represents the reliability factor, and its value is dependent on the number of parameters that are involved in the study. When an infinite number of parameters are studied, the maximum value of (f) is 1. However, as the number of parameters decreases, the value of (f) also decreases. For example, when studying 15 parameters, the value of (f) is 0.971. Similarly, for 12 parameters, the value of (f) is 0.952, and for 8 parameters, the value of (f) is 0.9.

Orally Disintegrating Tablets' Preparation

Each tablet contained 100 mg of vitamin C, 200 mg of a single selected excipient, and 1% (w/w) of magnesium stearate. The powder was mixed with a cubic mixer (Aymes, Turkiye) at 60 rpm for 5 min. For each tablet, a pre-weighed quantity of powder blend (303 mg) was manually introduced into the die prior to compression in an eccentric compression machine (Yeniyurt, Turkey) with convex face punches and a 6 mm diameter. The compression force was 500 psi and 750 psi unidirectional. Die filling by gravity was not involved, and tablet mass uniformity was independent of powder flow during the compression step.

Evaluation of Orally Disintegrating Tablets

Diameter and Thickness

Diameter and thickness of tablets ($n = 10$) were determined using a vernier caliper (Werka, Switzerland).

Weight Variation

Randomly, tablets ($n = 20$) from each formulation were weighed individually and precisely on a digital balance (Sartorius, Germany), and then the average weight was determined. After all, each tablet's deviation from the average value was recorded [31].

Tablet Breaking Force

The force required to cause tablets to break when crushed is the resistance to breakage [32]. The result is recorded in Newton using (Sotax HT, Switzerland) as the equipment used. The test was performed individually on tablets ($n = 3$).

Friability Test

The friabilator device (Aymes, Turkey) is the equipment used to assess friability. The procedure included removing dust and weighing tablets ($n = 10$), then placing them inside a friabilizer and rotating them 100 times at 25 rpm for 4 min. After completion, the tablets were removed, any loose dust was eliminated, and the tablets were precisely weighed [33]. The percentage of friability was determined by using the following Eq. 5.

$$\text{Friability} = \left[\left(\text{Initial weight} - \text{Final weight}\right) / \left(\text{Initial weight}\right)\right] \times 100 \quad (5)$$

Friability = [(Initial weight –Final weight)/(Initial weight)] x 100 [5].

Disintegration Time

The disintegration test was carried out on tablets (n = 3) using disintegration equipment (Sotax DT2, Germany) with 900 ml medium of distilled water at 37.0 ± 0.5 °C. According to European Pharmacopeia compliance, ODTs must disintegrate within 3 min [34].

Dissolution Studies

The dissolution test was carried out using the paddle method (the USP type II) dissolution test apparatus (Sotax AT2, Germany). The vessels were filled with 900 ml of phosphate-buffered solution (pH 6.8) used as a dissolution medium. The apparatus conditions were fixed at 37 °C ± 0.5 °C and the rotating paddles at 75 rpm. Samples were taken at different times (1, 3, 5, 10, 15, 20, 30, 45, and 60 min), and then passed through a filter (25 mm FLL/MLS PP ×0.45 µm Nylon, GVS, North America, USA) to remove undissolved compounds. Concurrently, an equal volume of dissolution medium was added to the vessels. Filtered samples were analyzed by a UV-VIS spectrophotometer (UV-1280; Shimadzu, Kyoto, Japan) at a wavelength of 266 nm. The method of analysis was validated according to the International Conference on Harmonization (ICH) Q2 guidelines. The dissolution test was performed on tablets (n = 3).

Results and Discussion

SeDeM-ODT Characterization of Vitamin C

Vitamin C is a water-soluble, odorless white powder; however, SeDeM-ODT analysis revealed that it is poorly suited for direct compression into orally disintegrating tablets. Low incidence factors were observed for Flowability, Compressibility, and Disgregability, all of which are critical attributes for direct compression. The compressibility factor was particularly low, indicating inadequate compactability and a high risk of friability, capping, or tablet breakage during compression [35]. Similarly, the low flowability factor reflects poor powder flow, which may compromise process robustness. Vitamin C also exhibited a low homogeneity index and a high proportion of fine particles (< 50 µm), indicating a cohesive powder with an elevated segregation risk. In contrast, the lubricity/stability factor showed acceptable values, consistent with the non-hygroscopic nature of the material. Despite its high aqueous solubility, the Disgregability factor was markedly low, indicating limited intrinsic self-disintegration capacity.

Overall, most SeDeM-ODT incidence factors for vitamin C were below the acceptance threshold ($r \geq 5$), resulting in a low IGCB value of 4.19, as seen in Fig. 1 and Table S2. These results confirm that vitamin C alone is unsuitable for direct compression ODT formulation and requires functional excipients to compensate for its deficient powder properties.

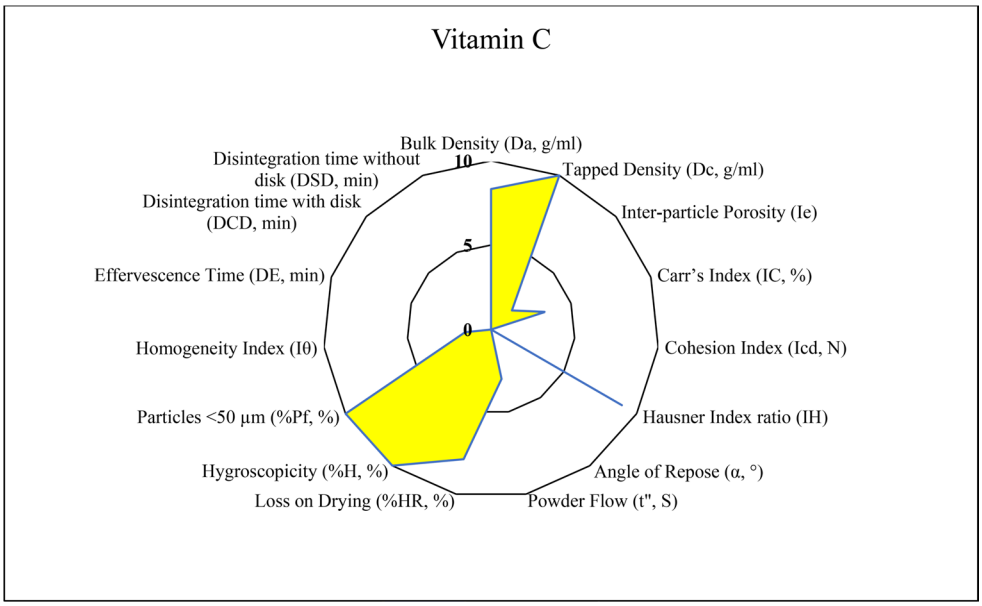

Fig. 1 SeDeM-ODT diagram of Vitamin C powder

SeDeM-ODT Characterization of Vitamin C-excipient Blends

To improve the direct compression suitability of vitamin C, both co-processed and single-component excipients were evaluated using the SeDeM-ODT expert system. Co-processed excipients (Prosolv® ODT G2, Parteck® ODT, Ludiflash®, and Ludipress® LCE) are commercially manufactured by physical co-processing techniques such as spray-drying or granulation, combining multiple excipients into a single composite particle without chemical modification. Single-component excipients (EMDEX®, Ceolus™ UF-702, and Ceolus™ UF-711) consist of chemically uniform materials manufactured via crystallization or controlled hydrolysis. The effects of these excipients are discussed below according to their dominant functional characteristics to facilitate comparison.

Co-processed ODT Excipients

Prosolv® ODT G2 exhibited acceptable SeDeM-ODT performance, with Dimension, Flowability/Powder flow, Lubricity/Stability, and Lubricity/Dosage factors exceeding the acceptance threshold ($r \geq 5$), whereas the Compressibility factor remained slightly below the limit (4.83), as shown in Table S2. This SeDeM-ODT profile reflects the functional contribution of its co-processed composition, which combines microcrystalline cellulose (MCC), colloidal silicon dioxide, mannitol, fructose, and crospovidone to support powder flow, compactibility, and disintegration-related attributes [36].

In the vitamin C–Prosolv® ODT G2 powder blend, improvements were observed in Flowability/Powder flow, Compressibility, Lubricity/Stability, and Lubricity/Dosage factors compared with vitamin C alone [5], as shown in Fig. 2. Nevertheless, compressibility remained below the acceptance threshold, and the Disgregability factor did not improve as expected for an excipient designed for orally disintegrating tablets. The Dimension factor decreased but remained above the acceptance limit. As a result, the IGCB value reached the minimum acceptable threshold (IGCB = 5.0), as presented in Table S3, indicating borderline suitability for direct compression ODT formulation.

The reduced Disgregability observed after incorporation of vitamin C suggests that the presence of the API adversely affected compact break-up behavior, leading to longer disintegration compared with Parteck® ODT-based formulations, despite similar excipient-level disintegration performance reported in the literature [37]. This highlights the API-dependent nature of excipient functionality and the importance of formulation-specific evaluation.

According to Table S2, Parteck® ODT exhibited high SeDeM-ODT values for Dimension, Flowability/Powder flow, Lubricity/Stability, and Lubricity/Dosage, whereas the Compressibility factor remained low (2.63). This SeDeM profile suggests that Parteck® ODT primarily contributes to improving powder flow and Disgregability-related parameters rather than compactability.

Parteck® ODT is composed of granulated D-mannitol and croscarmellose sodium, forming agglomerated particles with relatively uniform morphology. The granulated structure is consistent with the favorable flowability observed in the SeDeM-ODT analysis. Although its intrinsic compressibility is limited, fragmentation and partial plastic deformation of granulated mannitol may contribute to compact formation under direct compression conditions [36].

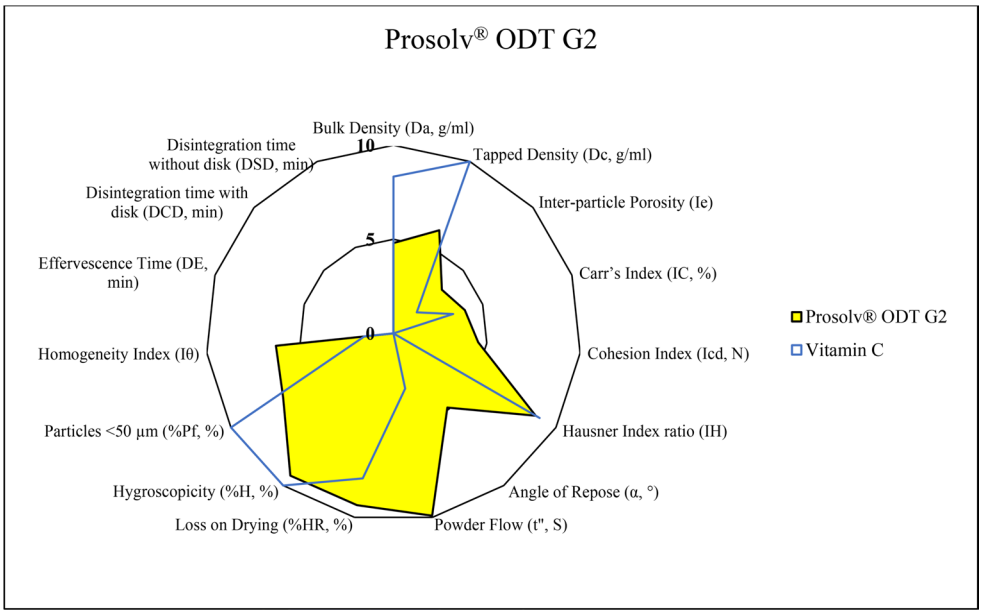

Fig. 2 SeDeM-ODT diagram of formula of Vitamin C and Prosolv® ODT G2 and Vitamin C powder

In the vitamin C–Parteck® ODT blend, all incidence factors except compressibility exceeded the acceptance threshold ($r \geq 5$), resulting in marked improvements in flowability and Disgregability compared with vitamin C alone. Despite the persistently low compressibility factor, the overall balance of properties yielded an IGCB value of 5.85, as shown in Table S3 and Fig. 3, indicating suitability for direct compression ODT development. As shown in Table S2, Ludiflash® exhibited high SeDeM-ODT values for Dimension, Compressibility, Lubricity/Stability, and Lubricity/Dosage, whereas the Flowability/Powder flow factor was slightly below the acceptance threshold (4.62). This profile indicates that Ludiflash® primarily contributes to improving compressibility rather than powder flow.

Ludiflash® is a co-processed excipient composed of non-agglomerated D-mannitol, crospovidone, and polyvinyl acetate. It is fine, plate-like particles and polydisperse nature result in high cohesiveness and limited flowability, consistent with the observed SeDeM flow parameters. The presence of polyvinyl acetate as an insoluble binder and crospovidone as a superdisintegrant supports compact formation and disintegration [36].

In the vitamin C–Ludiflash® formulation, marked improvements were observed in Flowability/Powder flow, Lubricity/Stability, Lubricity/Dosage factors compared with vitamin C alone, with all values exceeding the acceptance limit ($r \geq 5$). Despite the persistently low flowability and a reduction in the dimension factor, the overall balance of properties led to a substantial increase in IGCB to 6.04, as presented in Table S3 and Fig. 4. These results confirm that Ludiflash® effectively compensates for the poor compressibility of vitamin C and is suitable for direct compression ODT formulation, provided that flow limitations are managed during processing.

As shown in Table S2, Ludipress® LCE exhibited high SeDeM-ODT values for Dimension, Flowability/Powder flow, Lubricity/Stability, and Lubricity/Dosage, indicating strong flow-enhancing capability. In contrast, the Compressibility factor remained low (2.03), reflecting limited compactability.

Ludipress® LCE is a co-processed excipient composed primarily of lactose and povidone (Kollidon® 30). Lactose-based excipients are widely used in tablet formulations due to their high aqueous solubility and favorable processing characteristics [38]. Previous studies have also reported excellent flowability for Ludipress-based excipients, with Carr's index values below 15%, indicating good powder flow behavior [39]. However, the composition of Ludipress® LCE does not include a dedicated disintegrant component, which may limit its contribution to rapid tablet disintegration.

In the vitamin C–Ludipress® LCE formulation, improvements were observed in Flowability/Powder flow, Lubricity/Stability, and Lubricity/Dosage factors compared with vitamin C alone, with all three parameters exceeding the acceptance threshold ($r \geq 5$). However, Compressibility and Disgregability factors remained below the acceptable limit, and the dimension factor decreased slightly to 5.2, as seen in Table S3, Fig. 5. Despite an increase in IGCB to 5.52, the overall performance indicates that Ludipress® LCE enhances processability but provides limited support for disintegration, reducing its suitability as a standalone excipient for direct compression ODT formulation.

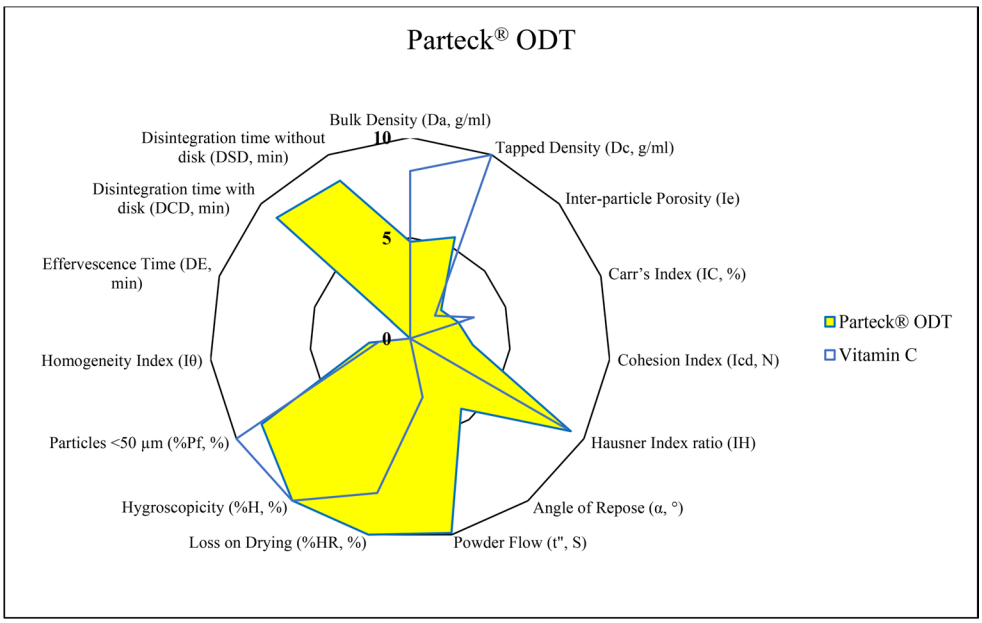

Fig. 3 SeDeM-ODT diagram of formula of Vitamin C and Parteck® ODT and Vitamin C powder

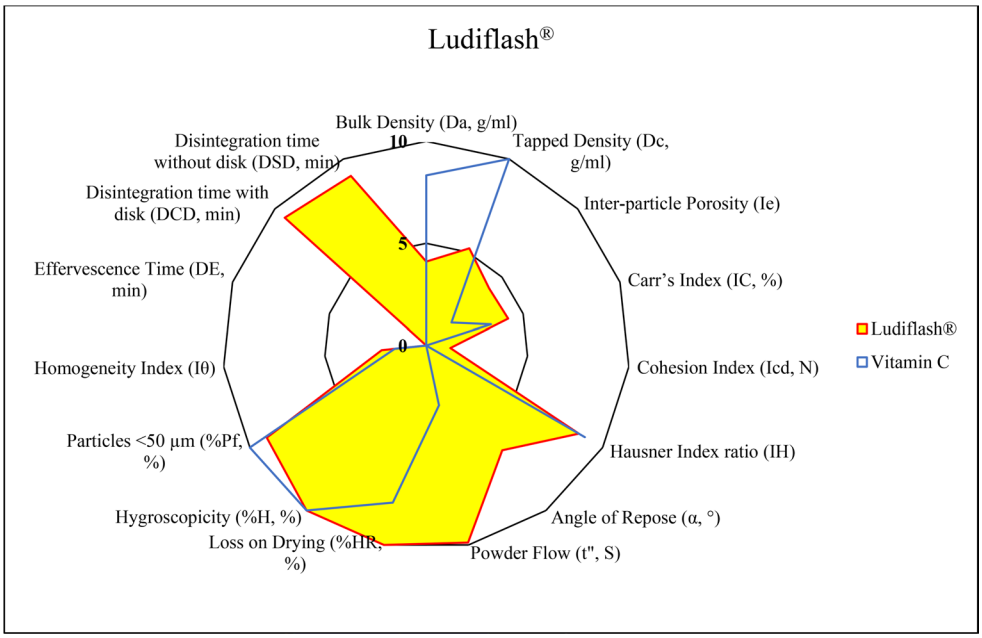

Fig. 4 SeDeM-ODT diagram of formula of Vitamin C and Ludiflash® and Vitamin C powder

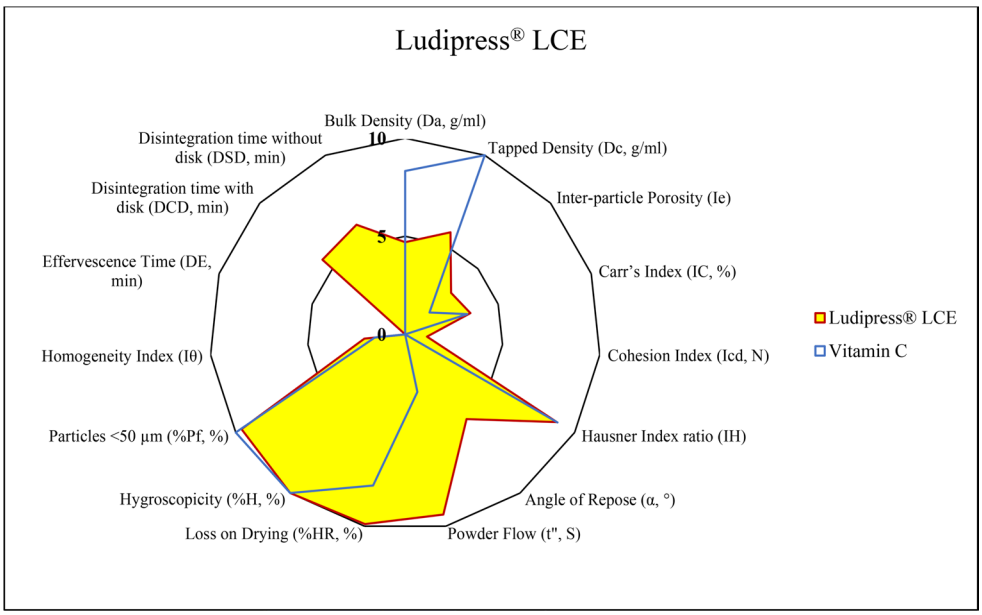

Fig. 5 SeDeM-ODT diagram of formula of Vitamin C and Ludipress® LCE and Vitamin C powder

Single-component Excipients

According to Table S2, EMDEX® exhibited high SeDeM-ODT values for Dimension, Flowability/Powder flow, Lubricity/Stability, and Lubricity/Dosage, confirming its effectiveness as a flow-enhancing excipient. In contrast, its Compressibility factor was extremely low (0.7), indicating very limited compactability.

EMDEX® is a highly water-soluble filler–binder composed predominantly of glucose monohydrate with minor oligosaccharide content derived from starch hydrolysis. This crystalline, non-deforming structure explains its favorable flow behavior but poor contribution to tablet cohesion [40].

In the vitamin C–EMDEX® formulation, flowability- and lubrication-related factors exceeded the acceptance threshold ($r \geq 5$); however, Compressibility and Disgregability remained below acceptable limits. Although slight improvements in these parameters were observed relative to vitamin C alone, the overall IGCB value remained low (4.47), as seen in Table S3 and Fig. 6. These findings indicate that, while EMDEX® improves powder handling, it is

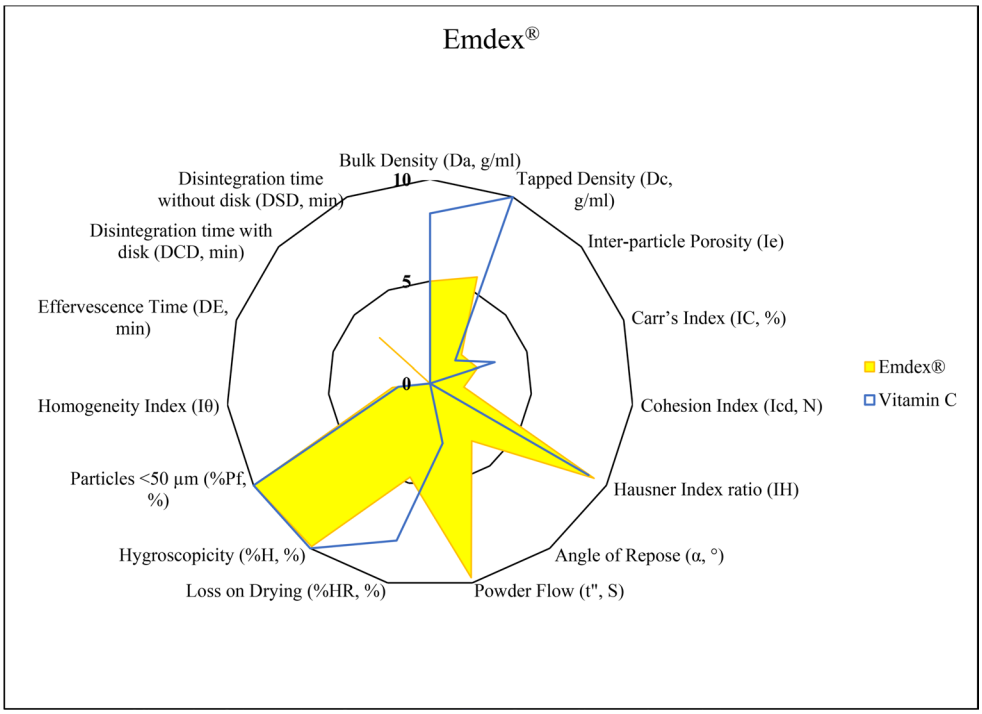

Fig. 6 SeDeM-ODT diagram of formula of Vitamin C and EMDEX® and Vitamin C powder

insufficient as a standalone excipient for direct compression ODT formulation due to inadequate compactability and disintegration performance.

As shown in Table S2, Ceolus™ UF-702 exhibited high SeDeM-ODT values for Compressibility, Lubricity/Stability, and Lubricity/Dosage, whereas the Dimension factor was low and Flowability/Powder flow was close to, but slightly below, the acceptance threshold. This profile indicates that Ceolus™ UF-702 primarily contributes to improving compressibility rather than flow behavior.

Ceolus™ UF-702 is a microcrystalline cellulose–based filler characterized by a spherical morphology and an average particle size of approximately 90 µm. Its relatively large, porous particles and low bulk density promote plastic deformation during compression, facilitating tablet formation and contributing to faster disintegration. However, these structural features also limit dimensional uniformity and only moderately improve flowability [41].

In the vitamin C-Ceolus™ UF-702 formulation, marked improvements were observed in Compressibility, Flowability/Powder flow, Lubricity/Stability, Lubricity/Dosage, and Disgregability factors relative to vitamin C alone. Although the Disgregability factor was close to the acceptance limit and the dimension factor decreased below 5, the overall balance of properties resulted in an IGCB value of 5.99, as seen in Table S3 and Fig. 7. These results indicate that Ceolus™ UF-702 is a suitable excipient for direct compression ODT formulation, primarily by compensating for the poor compactability of vitamin C.

As indicated in Table S2, Ceolus™ UF-711 exhibited high SeDeM-ODT values for Compressibility, Lubricity/Stability, and Lubricity/Dosage, whereas Dimension and Flowability/Powder flow remained below the acceptance threshold ($r < 5$). This profile suggests that Ceolus™ UF-711 primarily contributes to enhancing compressibility rather than powder flow.

Ceolus™ UF-711 consists of porous spherical microcrystalline cellulose agglomerates with an average particle size of approximately 50 µm and a low bulk density (0.22 g/cm³) [42]. These structural characteristics promote plastic deformation during compression, thereby improving tablet compactibility, but may also increase cohesiveness and limit flowability [43].

In the vitamin C–Ceolus™ UF-711 formulation, improvements were observed in Compressibility, Flowability/Powder flow, Lubricity/Stability, Lubricity/Dosage, and Disgregability factors relative to vitamin C alone. However, the Disgregability factor remained below the acceptable limit, and the dimension factor decreased to values < 5, as seen in Fig. 8. Despite these limitations, the overall SeDeM-ODT profile yielded an IGCB value of 5.46, as shown in Table S3, indicating that Ceolus™ UF-711 enables direct compression ODT formulation, albeit with less balanced performance compared to Ceolus™ UF-702.

Selection of Excipients for Tablet Preparation

Based on the SeDeM-ODT screening, excipients that achieved an IGCB > 5 and exhibited complementary functional profiles. Consequently, Ludiflash®, Parteck® ODT, and Ceolus™ UF-702 were chosen for further evaluation,

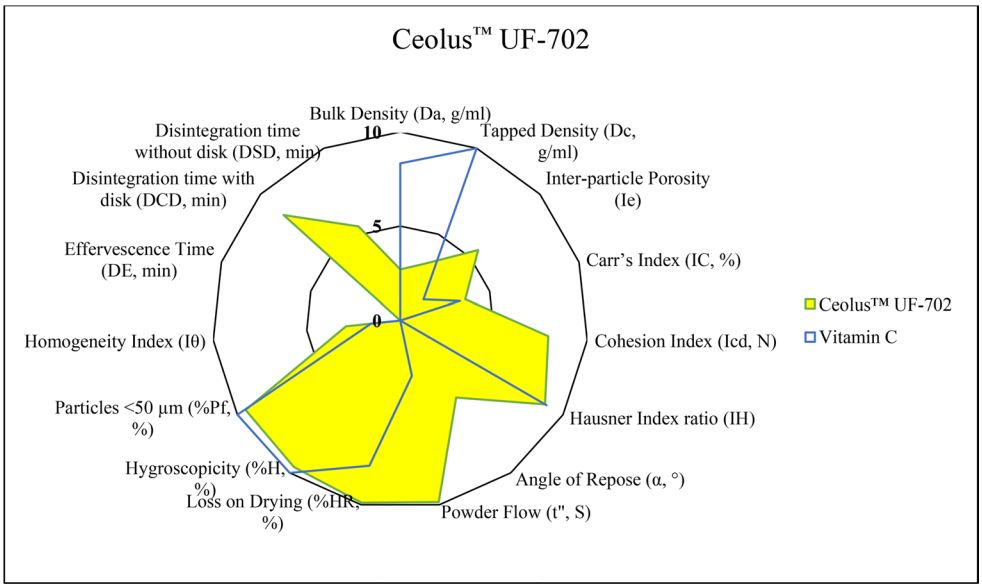

Fig. 7 SeDeM-ODT diagram of formula of Vitamin C and Ceolus™ UF-702 and Vitamin C powder

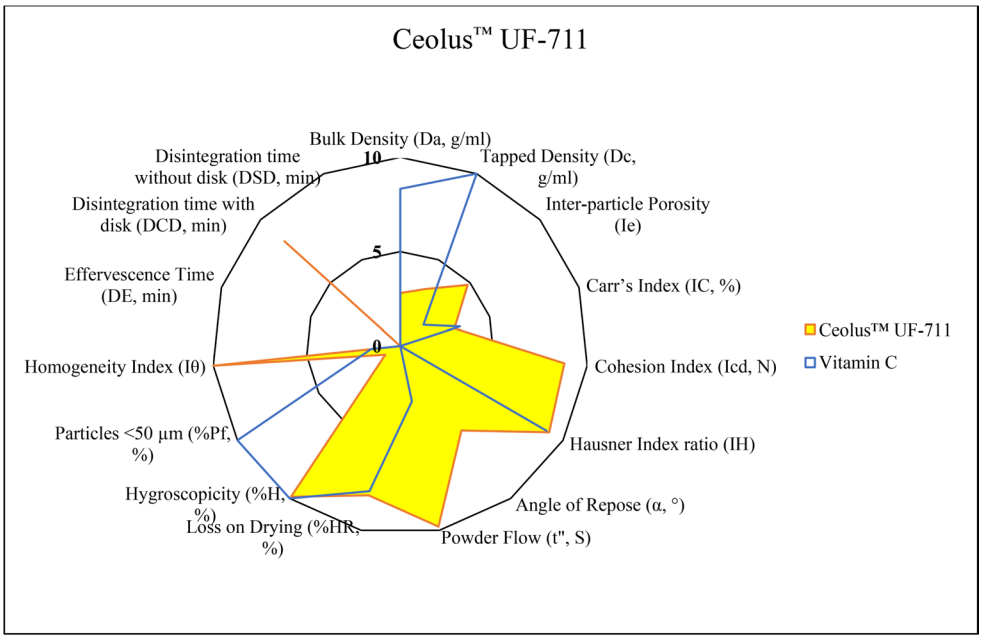

Fig. 8 SeDeM-ODT diagram of formula of Vitamin C and Ceolus™ UF-711 and Vitamin C powder

as they are suitable for preparing orally disintegrating tablets using the direct compression method. These excipients were selected for further tablet property tests. Each ODT contained 100 mg of vitamin C, 200 mg of excipient, and 1% magnesium stearate. The tablets were compressed at different forces (500 and 750 psi) to observe their disintegration time.

Evaluation of Orally Disintegrating Tablets

Ceolus™ UF-702 and Parteck® ODT tablets were found to have a low friability percentage, whereas Ludiflash® tablets showed a high friability percentage, as presented in Table 1. All three formulations showed a low friability percentage when subjected to high compression force (750 psi), which is within the acceptable limit of not more than 1.0%. This was expected as the SeDeM-ODT expert system had noted a high Cohesivity Index during the formulation powder characterization.

It is common knowledge that tablet thickness can vary even if the weight remains the same, due to differences in density or applied force during the compression process. Therefore, uniformity in tablet size can provide valuable information about the compression process [44]. Table S3 shows that all formulations in the study produced uniformly sized tablets with a low standard deviation of less than 1% for both thickness and diameter. Weight variation is also an important factor in determining the accuracy of

Table 1 Characterization of the ODT formulations at different compression forces

500 psi						
Formulations	Thickness (mm)	Diameter (mm)	Tablet Breaking Force (N)	Weight Variation (mg)	Friability Test (%)	Disintegration Test (s)
Ceolus™ UF-702	4.77	8.73	101.60	298.15	0.12	34.00
SD	0.03	0.00	8.37	2.22		0.00
RSD	0.72	0.05	8.23	0.74		0.00
Parteck® ODT	4.89	8.92	53.00	298.08	0.38	16.30
SD	0.03	0.18	5.88	3.68		1.15
RSD	0.73	2.05	11.10	1.23		7.06
Ludiflash®	4.71	8.74	26.00	293.10	1.08	12.30
SD	0.07	0.00	1.41	2.73		0.57
RSD	1.52	0.09	5.43	0.92		4.68
750 psi						
Formulations	Thickness (mm)	Diameter (mm)	Tablet Breaking Force (N)	Weight Variation (mg)	Friability Test (%)	Disintegration Test (s)
Ceolus™ UF-702	4.45	8.71	133.66	299.90	0.33	49.00
SD	0.02	0.00	22.00	1.74		2.50
RSD	0.56	0.05	16.46	0.58		5.10
Parteck® ODT	4.70	8.68	105.00	298.98	0.53	31.60
SD	0.09	0.01	4.96	2.40		7.60
RSD	2.07	0.16	4.73	0.87		4.68
Ludiflash®	4.54	8.72	47.66	295.67	0.40	19.30
SD	0.03	0.01	4.45	2.50		1.15
RSD	0.73	0.14	9.43	0.87		24.10

dosage and the quality of the compression process [45]. The weight variation of all the tablets met the criteria of the USP, which requires a percentage difference of no more than 7.5% [46]. Although tablet weight variation was within pharmacopeial limits for all formulations, it should be noted that the use of a single-punch tablet press with manual die filling bypasses gravity-controlled powder flow. Therefore, SeDeM flowability parameters are discussed in this study as predictive indicators of material suitability for direct compression at an industrial scale, rather than as direct determinants of tablet mass uniformity under the present experimental conditions.

The disintegration time of ODTs is a crucial factor, which is directly influenced by their tablet breaking force. The uniformity of the in-process material and the compression force used are the primary factors that determine the tablet breaking force [47]. Ideally, ODTs should have a low tablet breaking force, with a minimum of 25 N being acceptable [48]. Ceolus™ UF-702, Parteck® ODT, and Ludiflash® provided acceptable tablet breaking force at different compression forces.

All three formulations exhibit ideal disintegration time for ODTs, indicating that the selection of excipients and amounts was accurate. Ceolus™ UF-702, Parteck® ODT, and Ludiflash® meet the European Pharmacopeia criteria for acceptable disintegration time (within 3 min). It has been noticed that Parteck® ODT exhibited high tablet breaking force with low disintegration time, which was preferable and in accordance with the SeDeM-ODT expert system, as presented in Table 1.

The USP [49] guideline was followed to carry out the dissolution test of the formulations to determine if ODT dissolves Q ≥ 75% in 45 min. It should be noted that while disintegration was assessed under aqueous conditions relevant to the oral cavity, dissolution testing was conducted in phosphate buffer pH 6.8 to reflect post-swallow gastrointestinal conditions and comply with pharmacopeial practice. Upon analyzing Fig. 9, it can be observed that the formulations comply with this requirement. However, Ceolus™ UF-702 attained a plateau within 5 min at 500 psi and 750 psi compression force. Parteck® ODT reached a plateau (Q > 90%) within 3 min at different compression forces. Ludiflash® reached a plateau within 10 min at 500 psi, while taking 15 min to reach a plateau at 750 psi. The drug release profiles were generally comparable at both compression forces. However, a slightly slower release was observed for Ludiflash® at 750 psi compared with 500 psi, which may be associated with the higher tablet density produced at increased compression pressure.

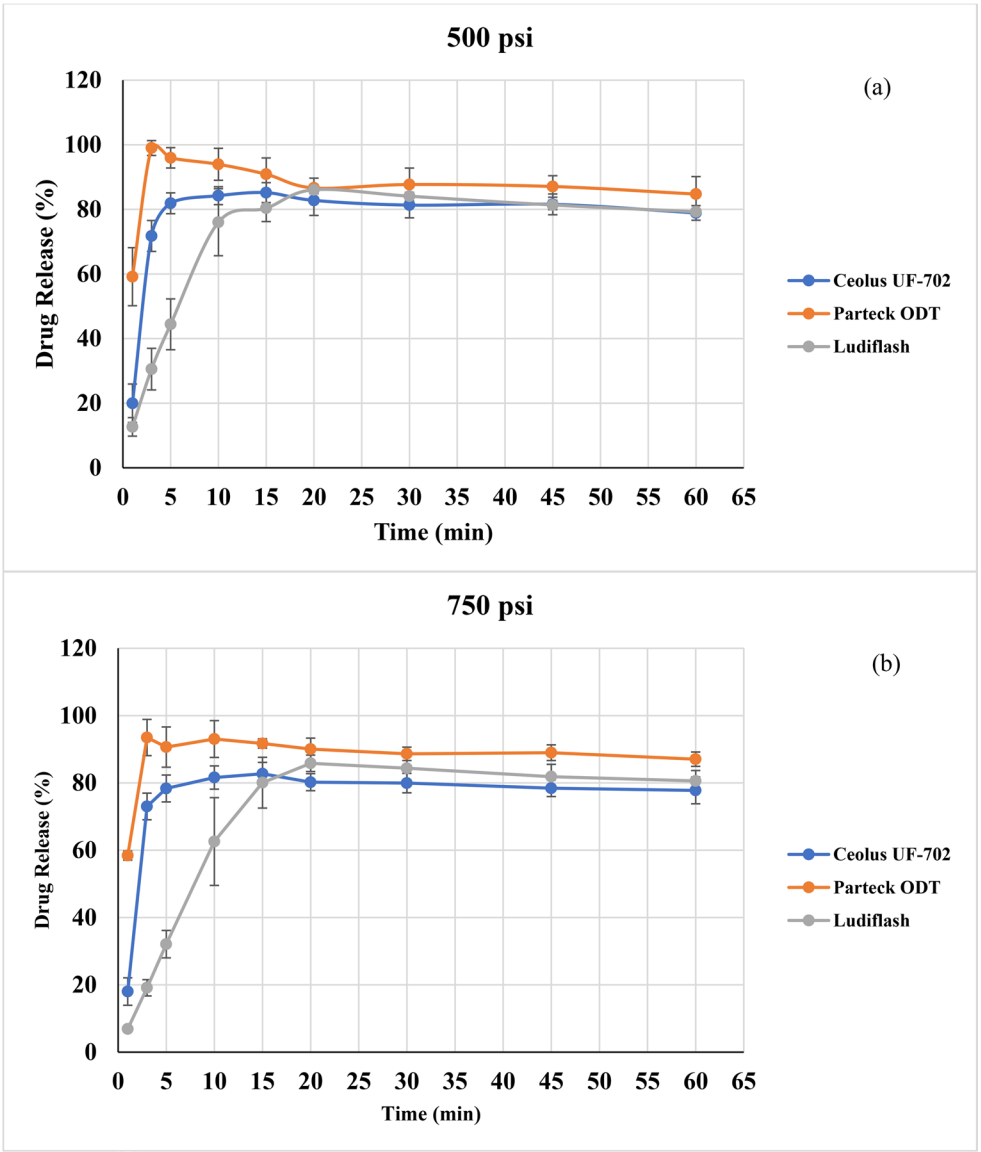

Fig. 9 Dissolution profile of the ODT formulations: **a** 500 psi compression force, **b** 750 psi compression force (mean ± SD, $n = 3$)

A slight decrease in the dissolution profiles at later sampling points can be observed. Although such behavior could be interpreted as precipitation of the dissolved drug, this explanation is unlikely for vitamin C due to its high aqueous solubility at pH 6.8. A more plausible explanation is the known instability of ascorbic acid in aqueous media, where gradual oxidative degradation may occur during extended dissolution testing.

Data Availability and Reproducibility Statement

The methodology known as SeDeM-ODT is composed of six factors based on 15 main parameters. These six factors, namely dimensions, compressibility, flowability/powder flow, lubricity/stability, lubricity/dosage, and Disgregability, are calculated using experimental studies and quantitative determination of the characterization parameters of substances in powder form. The results of these calculations provide essential information about the suitability of the substances for direct compression technology, which is used to obtain tablets. Table S1 presents the parameters listed below are commonly referred to as Bulk Density (Da, g/ml), Tapped Density (Dc, g/ml), Inter-particle Porosity (Ie), Carr's Index (IC, %), Cohesion Index (Icd, N), Hausner Index ratio (IH), Angle of Repose (α, °), Powder Flow (t", S), Loss on Drying (%HR, %), Hygroscopicity (%H, %), Particles < 50 µm (%Pf, %), Homogeneity Index (Iθ), Effervescence Time (DE, min), Disintegration time with disk (DCD, min), and Disintegration time without disk (DSD, min). These parameters are determined using the SeDeM-ODT Diagram method, based on known equations in Table S1.

The SeDeM-ODT expert system is a new tool that can be used to determine whether a powdered excipient can be compressed into bucodispersable tablets. It calculates the Index

of Good Compressibility and Bucodispersibility (IGCB) for the candidates and assigns a ≥ 5 rating if the powder can be compressed through direct compression and has good bucodispersible properties. Additionally, it provides three numerical indexes to express whether the excipient can be used in making compressed ODT. These indexes include the index parameter (IP), the profile index parameter (IPP), and the IGCB. By calculating these indexes, SeDeM-ODT can more accurately select the excipients that can be used to make compressed ODT.

Table S1 in the Supplementary Material displays the parameters and equations employed by the SeDeM-ODT expert system. Table S2 presents parameters, such as radius, incidence factor, and parametric index, for powders that do not contain vitamin C. Additionally, the numerical data from Figs. 1, 2, 3, 4, 5, 6, 7 and 8, which show powders with vitamin C, are tabulated in Table S3 in the Supplementary Material.

After conducting tests on SedeM-ODT, it was found that Ludiflash®, Parteck® ODT, and Ceolus™ UF-702 are suitable excipients for preparing orally disintegrating tablets using the direct compression method. Further tests were conducted on these excipients to determine their tablet properties. Each ODT consisted of 100 mg of vitamin C, 200 mg of excipient, and 1% magnesium stearate. The tablets were compressed at different forces (500 and 750 psi) to observe their disintegration time, as the disintegration test is critical for ODTs. The tablets were characterized for their physical properties, including Thickness (mm), Diameter (mm), Tablet Breaking Force (N), Weight Variation (mg), Friability Test (%), Disintegration Test (s), and Dissolution Test (%). The numerical data presented in Fig. 9 have been compiled in Table S4 of the Supplementary Material. Error bars, where shown in Fig. 9, represent the spread of data observed in triplicate measurements. Table 1 provides the details of the ODT formulations at different compression forces.

Conclusion

This study applied the SeDeM-ODT expert system as a systematic preformulation tool to evaluate the suitability of several excipients for the development of vitamin C orally disintegrating tablets (ODTs) by direct compression. SeDeM-ODT analysis demonstrated that vitamin C powder alone exhibits inadequate flowability, compressibility, and disintegrability, resulting in a low IGCB value and confirming its unsuitability for direct compression without functional excipients.

Among the investigated materials, Ludiflash®, Parteck® ODT, and Ceolus™ UF-702 achieved IGCB values above the acceptance threshold (IGCB ≥ 5) and were therefore selected for tablet formulation studies. Tablets prepared with these excipients demonstrated acceptable physical properties, including uniform weight, adequate mechanical strength, and disintegration times well within the pharmacopeial limit for ODTs. Dissolution studies confirmed rapid drug release, with all formulations meeting the pharmacopeial requirement of Q ≥ 75% within 45 min, while also showing rapid early-stage release consistent with ODT performance. Although Ludiflash® showed slightly elevated friability at lower compression pressure, acceptable mechanical integrity was achieved at optimized compression conditions, while maintaining rapid disintegration. Overall, the results confirm that SeDeM-ODT provides a reliable screening framework for excipient selection in direct compression ODT development, enabling identification of excipients capable of compensating for the poor tableting properties of challenging APIs such as vitamin C.

These findings demonstrate that Ludiflash®, Parteck® ODT, and Ceolus™ UF-702 are suitable candidates for the formulation of vitamin C ODTs by direct compression, while further formulation optimization may enhance mechanical robustness and processing performance.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12247-026-10623-w.

Authors' contributions All authors participated in preparing and reviewing the manuscript.

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Data Availability No datasets were generated or analysed during the current study.

Declarations

Ethical approval An animal study is not applicable to this article.

Competing interests The authors declare no competing interests.

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