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Simplex Lattice Optimization of Purple Sweet Potato Leaf Extract Tablets with PVP K30 and Croscarmellose Sodium

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ABSTRACT

Purple sweet potato leaves (*Ipomoea batatas* L.) are rich in flavonoids with antidiabetic potential. This study optimized a tablet dosage form of the leaf extract using a Simplex Lattice Design (SLD) with PVP K30 (2–5%, binder) and croscarmellose sodium (3–5%, superdisintegrant). Eight wet-granulated formulations (520 mg/tablet; 240 mg extract) were evaluated for hardness, friability, and disintegration time. SLD models and contour plots guided numerical optimization targeting hardness 4–8 kp, friability <1%, and disintegration <15 min. The optimal composition—5% PVP K30 + 3% croscarmellose sodium—achieved hardness 6.28 ± 0.05 kp, friability 0.17 ± 0.01%, and disintegration 05:20–07:45, meeting pharmacopeial criteria. Verification (three independent batches) fell within prediction ranges with overall desirability = 1.0. These findings support the binder–superdisintegrant system for robust herbal tablets of purple sweet potato leaf extract; dissolution and stability testing are recommended in future work.

Keywords:
Purple sweet potato leaves; PVP K30; Croscarmellose sodium; Simplex lattice design; Tablet optimization

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1. Introduction

Purple sweet potatoes are easily available plants, with the tubers being used by the community as food, but the leaves are often underutilized as animal feed or discarded as waste. This study utilises sweet potato leaves as an alternative for antidiabetic treatment. This potential is mainly due to their high flavonoid content, which possesses antioxidant and antidiabetic activities. The flavonoid content in purple sweet potato leaves is higher than in other sweet potato varieties, such as those with yellow or white leaves, making them more suitable for use as raw material for herbal tablets [1]. In addition, purple sweet potato leaves are abundant in Indonesia and easy to cultivate, making them an economical and sustainable source of natural ingredients for the development of phytopharmaceuticals.

A dose of 300 mg/kgBW of 96% ethanol extract of purple sweet potato leaves can reduce blood sugar levels in male rats by 71.34% in 14 days [2]. A combination of purple sweet potato leaf extract and insulin leaves can reduce blood glucose levels in rats at a dose of 120 mg/kgBW, with an average reduction in blood glucose levels of 42.27 mg/dL

[3]. Therefore, the dose used in this study was 300 mg/kgBW of 96% ethanol extract of purple sweet potato leaves according to Haryoto, as the dose according to Yosephine required a combination with insulin leaves.

Herbal medicine preparations need to be developed to improve their practicality in use. Purple sweet potato leaf extract was made in the form of a simplisia, such as tea, but this form of herbal medicine preparation could not mask the distinctive smell of purple sweet potato leaves [4]. One way to overcome this is to make it into tablets, which have several advantages, such as being easy to consume, practical, and accurate in dosage. Tablets are solid dosage forms containing active ingredients with or without excipients [5].

One excipient that must be considered to obtain good tablets is a binder and disintegrant. The use of PVP K30 as a binder has the advantage of producing granules with relatively good flow rate, resulting in a minimum angle of repose, producing granules with fine particles, resistant to moisture, and good compactibility. Its mechanism allows water in the air to be absorbed into the tablet, reducing its ability to expand when in contact with a liquid medium, thereby resulting in a longer tablet disintegration time [6]. Croscarmellose sodium is used as a disintegrant because it is a good absorbent, a material that can enhance drug dissolution, and is effective in both direct compression and wet granulation formulations. Croscarmellose sodium has a primary mechanism of swelling, expanding 4-8 times its original size, enabling the tablet formulation to disintegrate rapidly [7].

Several studies related to the use of PVP K30 binding agents have produced satisfactory evaluations, namely at concentrations of 2% [8], 3% - 5 % [9]. Several studies related to the use of Croscarmellose sodium disintegrant produced hardness, friability, and disintegration time that met the requirements, namely a concentration of 3%[10], a concentration of 4% [11], and a concentration of 5%[12]. An active ingredient must go through the preformulation and formulation stages. One of these stages is formulation, which requires design and strategy through optimisation using the Simplex Lattice Design (SLD) method to produce a high-quality product. Optimization of formulation plays a crucial role in the standardization of herbal products, ensuring consistent quality, safety, and efficacy. The simplex sattice design (SLD) supports this process by minimizing the number of required trials and enhancing predictive accuracy in identifying optimal formulation parameters. SLD is a technique for predicting the profile of mixture properties. This profile is used to predict the composition of ingredients that provide optimum properties[13]. Based on this description, this study was conducted by formulating the optimisation of purple sweet potato leaf extract tablets using variations in the concentration of PVP K30 as a binding agent, namely concentrations of 2%-5%, and variations in the concentration *of* Croscarmellose sodium as a disintegrant, namely concentrations of 3%-5% using the simplex lattice design method based on the physical properties of the preparation, including hardness, friability, and disintegration time tests.

2. Method

Preparation of Raw Materials

A total of 16 kg of fresh purple sweet potato leaves (*Ipomoea batatas* L. Poir.) were collected in Cijambe Village, Sukabumi Regency, West Java. Botanical identification was performed at PT Palapa Muda Perkasa, Gg. Ceplik, Kalimulya, Cilodong District, Depok City, West Java. Damaged leaves were removed, the material was drained, then oven-dried at 40 °C for 7–8 h to limit degradation of heat-sensitive flavonoids. The dried

material was milled and passed through a 40-mesh sieve to obtain a uniform powder. The powdered simplicia was stored in tightly closed, light-protected containers with silica gel [14].

Production of Purple Sweet Potato Leaf Extract

Powdered simplicia (4 kg) was divided into eight 500-g portions (amber maceration bottles). Each portion was macerated with 96% ethanol using three successive solvent portions per bottle—1.75 L, 1.05 L, and 0.70 L—over a total of 48 h, with solvent renewal every 16 h and manual agitation every 4 h at room temperature. Combined filtrates were concentrated by rotary evaporation under reduced pressure (50 °C) and further dried in a hot-air oven at 40 °C to obtain a solid extract, stored airtight and protected from light until use [15].

Extract Content Analysis (Total Flavonoid Content of the extract)

A 240 mg aliquot of dry extract was diluted to 25 mL with methanol and shaken for 10 min. Then 2.5 mL of this solution was transferred to a 25-mL volumetric flask; 1 mL of 10% $AlCl_3$ and 1 mL of 1 M sodium acetate were added and the solution was made up to volume with distilled water. After 20 min incubation, absorbance at 427 nm was measured and total flavonoid content (TFC) was calculated from the quercetin calibration curve (regression equation and r^2 reported), expressed as mg quercetin equivalents per gram (mg QE/g) [16]. Formula:

$$mg\ QE/g = [(A - b)/m] \times (V/M) \times DF,$$

where A = absorbance, m = slope, b = intercept, V = final volume (mL), M = sample mass (mg), DF = dilution factor.

Formulation and Tablet Preparation

Tablet formulation

Eight formulations were prepared combining PVP K30 (binder, 2–5%) and croscarmellose sodium (CCS; superdisintegrant, 3–5%) as defined by Design-Expert v13. Each tablet contained 240 mg leaf extract (46% w/w) with a target tablet weight of 520 mg. Microcrystalline cellulose (Avicel PH102) q.s. to 100%, talc 2% (glidant), and magnesium stearate 2% (lubricant) were used (see **Table 1**).

Table 1. Composition of purple sweet potato leaf extract tablets (percent w/w)

Ingredient	Function	F1	F2	F3	F4	F5	F6	F7	F8
Purple sweet potato leaf extract	Active ingredient	46.0	46.0	46.0	46.0	46.0	46.0	46.0	46.0
PVP K30	Binder	3.0	4.0	5.0	4.0	3.5	5.0	4.5	3.0
Croscarmellose sodium (CCS)	Superdisintegrant	5.0	4.0	3.0	4.0	4.5	3.0	3.5	5.0
Avicel PH102 (MCC)	Filler (q.s. to 100%)	42.0	42.0	42.0	42.0	42.0	42.0	42.0	42.0
Talc	Glidant	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Magnesium stearate	Lubricant	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0

Notes:
Total per formula = 100% w/w; each tablet 520 mg contains 240 mg extract (46% w/w). Because PVP+CCS = 8% in all formulas, Avicel PH102 = 42% consistently.

Wet-granulation process and compression

All ingredients were weighed per the formula. PVP K30 was dissolved in 70% ethanol (1:5 w/v) and used after complete dissolution. The internal phase (extract, CCS, Avicel PH102) was blended until homogeneous; binder solution was added gradually until massing. The wet mass was screened through 8-mesh, dried at 50 °C until dry granules formed, and re-screened through 16-mesh. The outer phase (talc and

magnesium stearate) was blended thoroughly, and the granules were compressed on a single-punch press (flat, Ø 10 mm) targeting tablet hardness 4–8 kp [18].

Tablet Quality Evaluation

Tablet observation is conducted using the five senses, including colour, shape, surface, detection of physical defects, and taste. Weight uniformity (n = 20) was assessed and interpreted against pharmacopoeial limits (Column A/Column B) [17]. Dimensions (n = 20)—thickness and diameter—were measured by vernier caliper; as a guideline, diameter should not exceed 3× and not be less than 1⅓× the thickness [17]. Hardness (n = 10) was determined with a tablet hardness tester and reported in kp, with a prespecified target of 4–8 kp [18]. Friability used whole tablets equivalent to approximately 6.8 g for the 520-mg dosage strength, rotated at 25 ± 1 rpm for 4 min; friability (%) was calculated as mass loss and required to be < 1% [17]. Disintegration (n = 6; up to 12 additional if required) was measured in 900 mL water at 37 ± 2 °C with one disk per tube; uncoated tablets were required to disintegrate within 15 min [17]. Unless otherwise specified, data are presented as mean ± SD.

Total Flavonoid Content in Tablets

A composite of 20 tablets was finely powdered. An amount equivalent to 240 mg extract was transferred to a 25-mL volumetric flask and brought to volume with methanol, then stirred on a magnetic stirrer for 20 min. Subsequently, 2.5 mL was transferred to a 25-mL flask; 1 mL of 10% $AlCl_3$ and 1 mL of 1 M sodium acetate were added and the solution was brought to volume with water. After 20 min incubation, absorbance was read at 427 nm and TFC was calculated using the same equation described in Section 2.3, expressed as mg QE/g [16].

Experimental Design, Optimisation, and Data Analysis

A mixture (Simplex Lattice) design was employed in Design-Expert v13 with the simplex lattice design (SLD) method, with factors A = PVP K30 (2–5%) and B = CCS (3–5%). Responses were hardness (kp), friability (%), and disintegration time (min). Numerical optimisation targeted hardness 4–8 kp, friability < 1%, and disintegration < 15 min, and reported overall desirability. Models were used to generate equations and contour plots for each response; the suggested optimum was reproduced in three independent batches (200 tablets each) and re-tested. Verification was considered acceptable when observed values fell within the software's prediction range, consistent with the Results section.

3. Result and Discussion

Determination of Total Flavonoid Content in Extract

Total flavonoid content (TFC) of the dry extract was measured using the $AlCl_3$ colorimetric method with quercetin as the reference standard [16]. The quercetin–$AlCl_3$ complex exhibited a maximum wavelength (λmax) of 427 nm; absorbance readings for the working standards fell within the Beer–Lambert window (0.2–0.8), including a representative value of 0.359 at 427 nm. An incubation-time study showed that 20 minutes produced a stable colour complex at 427 nm, which was used for all subsequent measurements.

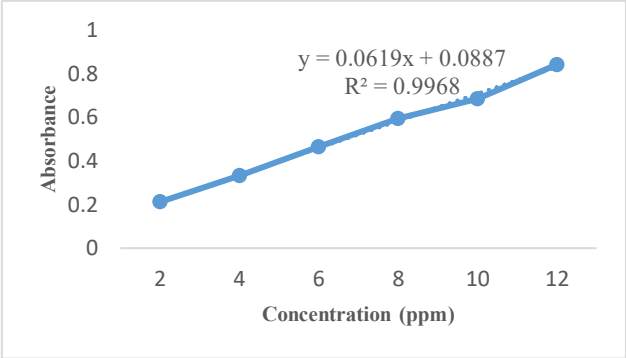

Figure 1. Quercetin calibration curve (λ 427 nm; 20-min incubation)

A calibration curve was prepared from a 100 ppm quercetin stock to yield 2, 4, 6, 8, 10, and 12 ppm working standards. Absorbance increased linearly with concentration, giving the regression y = 0.0619x + 0.0887 with R^2 = 0.9968 (**Figure 1**). Using this calibration, the TFC of the dried purple sweet-potato leaf extract was calculated as 6.1067 mg QE/g (mg quercetin equivalents per gram).

For context, a previous report by Anisa (2019) found TFC values for purple sweet-potato leaf ethanol extracts in the range 6.9648–9.8961 mg QE/g. The modest difference from our value may reflect raw-material variability (cultivar/leaf maturity, agroclimatic and harvest conditions) and pre-analytical handling (drying and sampling before analysis), rather than analytical discrepancies, as identical wavelength and incubation parameters were applied here [16].

Production of Purple Sweet Potato Leaf Extract Tablets

Eight tablet formulations were prepared, each weighing 520 mg/tablet, with 200 tablets per formulation, containing 240 mg (46%) of purple sweet potato leaf extract per tablet. The differences between each formulation lie in the addition of PVP K30 binder and Croscarmellose sodium disintegrant, which have been optimised using the simplex lattice design method. The tablets were produced using the wet granulation method. The purpose of using the wet granulation method is to improve the flow properties and compactibility of the ingredients, increase compressibility so that the tablets are easier to produce, and improve the distribution uniformity of the content. This resulted in good tablets that were not brittle, had good flow rates and good compactibility [18].

Tablet Quality Evaluation

Organoleptic Test

As shown in **Table 2**, all eight formulations exhibited uniform appearance: dark-green colour, round biconvex shape, a characteristic odour, and bitter taste, with no visible defects such as capping, chipping, lamination, or sticking. These findings satisfy the pharmacopoeial expectation that tablets possess a consistent colour, shape, and intact surface prior to further physical testing [17].

Table 2. Organoleptic characteristics of purple sweet potato leaf extract tablets (all eight formulations)

Attribute	Observation (n = 8 formulations)
Colour	Dark green, uniform (no mottling)
Shape / surface	Round, biconvex (convex surface)
Odour	Characteristic
Taste	Bitter
Visible defects	None observed (no capping, chipping, lamination, sticking)

From a formulation standpoint, the absence of macroscopic defects suggests that the wet-granulation and compression steps produced adequate inter-particle bonding and lubrication, supporting good handling characteristics during subsequent tests (weight variation, dimensions, hardness, friability, and disintegration). In other words, the organoleptic outcomes provide face-valid evidence that manufacturing parameters were appropriate and that the samples were suitable for quantitative quality evaluation according to the pharmacopoeial framework [17].

Weight Uniformity

As shown in **Table 3**, mean tablet weights for all eight formulations were tightly clustered at 522–525 mg with SD ≤ 3.8 mg and CV 0.51–0.73%, well within the ≤2% variability commonly accepted for this assay. These data, together with the narrow weight ranges (515–531 mg), indicate compliant weight variation under the Farmakope Indonesia acceptance scheme (evaluation against Column A/Column B limits) [17]. In practical terms, the low CV values imply consistent die filling and satisfactory flow/packing of the wet-granulated blend during compression.

Table 3. Weight uniformity and tablet flavonoid content ranges

Formula (PVP K30 : CCS)	Weight Range (mg)	Average Weight (mg) ± SD	CV (%)	Flavonoid Content Range of Tablets (%)
1 (3% : 5%)	515.2 – 526.8	521.60 ± 3.47	0.66	78.43 – 80.36
2 (4%: 4%)	516.3 – 527.6	522.09 ± 2.84	0.54	91.35 – 93.25
3 (5%: 3%)	518.2 – 527.2	523.40 ± 3.68	0.51	79.70 – 81.21
4 (4%: 4%)	521.2 – 529.8	524.65 ± 3.14	0.59	72.25 – 73.65
5 (3.5% : 4.5%)	519.8 – 528.2	524.18 ± 2.87	0.54	74.13 – 75.30
6 (5%: 3%)	518.2 – 529.2	523.44 ± 3.80	0.72	82.65 – 84.24
7 (4.5% : 3.5%)	518.9 – 529.3	522.96 ± 3.82	0.73	81.99 – 83.60
8 (3% : 5%)	517.9 – 530.8	524.22 ± 3.52	0.68	78.77 – 80.74

The final column in the flavonoid content range in tablets, calculated using the quercetin calibration described in Section 3.1. Most formulations maintained values ≥75%, whereas F4 (72.25–73.65%) and F5 (74.13–75.30%) trended at or slightly below the L1 threshold (≥75% for the initial 10 units) cited in the national guidance, suggesting a potential content distribution issue despite compliant weight variation [16],[19]. A plausible explanation is the hygroscopic nature of the extract, which can introduce small inconsistencies during weighing and blending; this interpretation aligns with the observation that mass variability remained low while the marker-content range dipped near the cutoff in those two formulas. Overall, the batch set fulfills pharmacopoeial expectations for weight uniformity, providing a sound basis for subsequent assessments of dimensions, hardness, friability, and disintegration [17],[18].

Size Uniformity

As summarised in **Table 4**, tablet thickness across all formulations clustered at 0.46–0.48 cm (mean ± SD as shown), while diameter was constant at 1.25 ± 0.00 cm. Applying the pharmacopoeial criterion that diameter must be ≥1⅓× and ≤3× the thickness, the calculated compliance ranges (rightmost column) fully encompassed the

observed diameter for every formula (e.g., thickness 0.46 cm → acceptable 0.61–1.38 cm; observed 1.25 cm), confirming that all batches met the dimensional requirement [17], [19].

Differences in PVP K30 (binder) and CCS (superdisintegrant) levels did not yield meaningful shifts in dimensions, which is expected because die size primarily determines diameter and compression pressure/fill uniformity primarily influence thickness—both held constant per Methods. The consistency of thickness and diameter supports the weight-uniformity findings and provides a stable geometric basis for subsequent mechanical (hardness, friability) and disintegration testing under the same pharmacopoeial framework [17].

Table 4. Size uniformity results

Formula (PVP K30 : CCS)	Thickness (cm) ± SD	Diameter (cm) ± SD	Acceptable diameter range (cm) *(1⅓×–3× thickness)*
1 (3% : 5%)	0.46 ± 0.02	1.25 ± 0.00	0.61–1.38
2 (4% : 4%)	0.46 ± 0.04	1.25 ± 0.00	0.61–1.38
3 (5% : 3%)	0.47 ± 0.04	1.25 ± 0.00	0.63–1.41
4 (4% : 4%)	0.47 ± 0.05	1.25 ± 0.00	0.63–1.41
5 (3.5% : 4.5%)	0.46 ± 0.03	1.25 ± 0.00	0.61–1.38
6 (5% : 3%)	0.47 ± 0.06	1.25 ± 0.00	0.63–1.41
7 (4.5% : 3.5%)	0.48 ± 0.05	1.25 ± 0.00	0.64–1.44
8 (3% : 5%)	0.46 ± 0.04	1.25 ± 0.00	0.61–1.38

Note : Acceptable diameter range = 1 ⅓× to 3× the reported thickness[17],[19]

The results of the eighth tablet size uniformity test met the requirements of the Indonesian Ministry of Health in 1979, namely that the tablet diameter should not be more than 3 times and not less than 1 1/3 times the tablet thickness. Differences in the concentration of binding agents and disintegrants did not result in significant differences in the size of the tablets produced, but could be influenced by the pressure applied during tablet compression. Uniform tablet diameter and thickness will affect the uniformity of tablet weight and active ingredients [19].

Tablet Hardness, Friability, and Disintegration Time

As summarised in **Table 5**, hardness values showed a clear mixture-dependent pattern. Formulae enriched with PVP K30 (binder) exhibited higher hardness—for example F3 and F6 (5% PVP K30 : 3% CCS) reached 7.47 ± 1.24 kp and 7.52 ± 1.11 kp, respectively—whereas high-CCS/low-binder mixtures such as F1 and F8 (3% : 5%) were at the lower end (3.97 ± 1.05 kp and 3.28 ± 0.47 kp). Most formulations satisfied the 4–8 kp target, with F1 and F8 falling below the prespecified threshold, consistent with their minimal binder level [18]. The overall trend aligns with the role of PVP K30 in strengthening inter-particle bonding and improving compactness during compression, thereby elevating tablet hardness at otherwise comparable press settings.

Friability results (**Table 5**) were uniformly compliant with the pharmacopoeial limit (<1%) across all eight formulations, ranging from about 0.20% (F6) to 0.70% (F8) [17]. As hardness increased, friability generally decreased (e.g., F3/F6: high hardness with 0.20–0.21% friability), reflecting stronger compacts that resist mechanical stress during handling and packaging. Conversely, formulations with lower hardness (e.g., F1/F8) showed relatively higher friability (0.66–0.70%) yet still well below the acceptance criterion, indicating that the wet-granulation and lubrication conditions provided adequate robustness even in low-binder mixtures.

Table 5. Summary of mechanical strength and disintegration

Formula (PVP K30 : CCS)	Hardness (kp) ± SD	Friability (%) ± SD	Disintegration (mm:ss) ± SD
1 (3% : 5%)	3.97 ± 1.05†	0.6646 ± 0.05	02:08 ± 0.51
2 (4% : 4%)	6.38 ± 1.05	0.3999 ± 0.001	05:27 ± 0.59
3 (5% : 3%)	7.47 ± 1.24	0.2021 ± 0.002	07:44 ± 0.26
4 (4% : 4%)	6.39 ± 0.94	0.3999 ± 0.001	05:17 ± 0.48
5 (3.5% : 4.5%)	4.24 ± 0.67	0.5052 ± 0.009	03:54 ± 0.61
6 (5% : 3%)	7.52 ± 1.11	0.1995 ± 0.0006	08:21 ± 0.71
7 (4.5% : 3.5%)	7.04 ± 1.22	0.3049 ± 0.01	06:32 ± 0.37
8 (3% : 5%)	3.28 ± 0.47†	0.7047 ± 0.008	02:29 ± 0.41

Note: † Below thehardness 4–8 kp [18]; friability <1% [17]; disintegration <15 min [17].

For disintegration, all uncoated tablets met the <15 min requirement in water at 37 ± 2 °C, with times reported as mm:ss (**Table 5**) [17]. As expected, higher CCS levels were associated with faster disintegration—notably F1 and F8 (3% : 5%) at approximately 02:08 and 02:29—while binder-rich mixtures disintegrated more slowly yet remained within specification (e.g., F3 07:44; F6 08:21). This pattern is consistent with wicking/swelling mechanisms of croscarmellose sodium that promote rapid fluid ingress and matrix breakup, whereas higher PVP K30 levels increase compactness and slightly delay water penetration.

Taken together, **Table 5** highlights the expected trade-off: increasing PVP K30 improves hardness and lowers friability, but tends to prolong disintegration; increasing CCS does the opposite—accelerating disintegration with a modest decrease in hardness. Within these opposing effects, several mixtures achieved a desirable balance that simultaneously satisfied the pharmacopeial criteria (hardness 4–8 kp, friability <1%, disintegration <15 min) [17],[18]. In particular, formulations at 5% PVP K30 : 3% CCS (F3/F6) delivered high hardness and very low friability while maintaining acceptable disintegration, making them strong candidates for the optimisation verified later in the SLD section.

Determination of Total Flavonoid Content in Tablets

Using the quercetin calibration described earlier (λ = 427 nm, 20 min incubation) [16], tablet TFC values ranged 4.42–5.64 mg QE/g across the eight formulations (**Table 6**). When normalised to the extract reference (6.1067 mg QE/g), this corresponds to 72.38–92.35% retention in the finished tablets. The highest retention was observed for F2 (4% : 4%) at 92.35%, while the lowest occurred for F4 (4% : 4%) at 72.38%; most other formulas clustered around 80–83%.

Table 6. Total flavonoid content of tablets and retention relative to extract

Formula (PVP K30 : CCS)	Flavonoid content of tablets (mg QE/g) ± SD	Flavonoid content of extract in tablet (%)	Complies L1 ≥ 75%
1 (3% : 5%)	4.85 ± 0.1098	79.42	Yes
2 (4% : 4%)	5.64 ± 0.3005	92.35	Yes
3 (5% : 3%)	4.92 ± 0.2462	80.56	Yes
4 (4% : 4%)	4.42 ± 0.1454	72.38	No
5 (3.5% : 4.5%)	4.56 ± 0.0001	74.68	No
6 (5% : 3%)	5.09 ± 0.1131	83.35	Yes
7 (4.5% : 3.5%)	5.04 ± 0.9895	82.53	Yes
8 (3% : 5%)	4.87 ± 0.1073	79.74	Yes

Interpreted against the acceptance used elsewhere in this study (initial ten-unit examination L1 ≥ 75%), F2, F3, F6, F7, F1, and F8 met or exceeded the threshold, whereas F4 (72.38%) and F5 (74.68%) trended at/just below the cutoff (Table 6) [17],[19]. Notably, weight uniformity for all batches showed tight CVs (≤ 0.73%, **Table 3**), suggesting that the few sub-threshold TFC values are unlikely due to gross mass variation. A more plausible explanation—consistent with our earlier discussion—is handling of a hygroscopic extract during weighing/blending and minor process effects during wet-granulation/drying, which can introduce small between-unit content fluctuations without materially affecting tablet mass.

The TFC data also align with the functional roles of the excipients examined here. PVP K30 (binder) strengthens inter-particle bonding and compactness (higher hardness, lower friability), which can help preserve phenolic content during mechanical handling; however, higher binder levels may marginally slow disintegration, necessitating balance with CCS (superdisintegrant), whose wicking/swelling accelerates breakup and promotes release [17],[18]. Literature likewise reports that PVP K30 can improve compact integrity (reducing fines and creating micro-cavities that help shelter actives), while increasing CCS may slightly reduce hardness but enhance disintegration and the accessibility of the active ingredient to the medium [20]. In our dataset, formulations with 5% PVP K30 : 3% CCS (F3/F6) combined high hardness, very low friability, acceptable disintegration (< 15 min), and ~81–83% tablet TFC—supporting their selection as strong candidates for optimisation/verification in the SLD section.

Simplex Lattice Design Results and Contour Plots

A Simplex sattice design (SLD) was applied to model the joint effects of PVP K30 (A) and croscarmellose sodium/CCS (B) on three tablet responses: hardness (kp), friability (%), and disintegration time. Mixture terms were interpreted under the usual constraint A + B = 1. The fitted mixture equations from Design-Expert v13 are summarised in **Table 7**, and the corresponding contour/overlay plots are shown in Figures 2–4. Overall trends align with the pharmacopoeial targets adopted in this study (hardness 4–8 kp, friability < 1%, disintegration < 15 min) [17],[18].

Table 7. Mixture-model equations from Design-Expert v13

Testing	Equation
Hardness (kp)	Y = 7.55 A + 4.69 B + 7.5476 AB
Friability (%)	Y = 0.198 A + 0.576 B − 0.202 AB
Disintegration time (s)	Y = 478.49 A + 201.46 B + 478.48 AB

Note: Y = response; A = fraction of PVP K30 component; B = fraction of Croscarmellose sodium component; AB = interaction between the two factors

For hardness (**Figure 2**), the model shows a stronger positive contribution from PVP K30 (A = +7.55) than from CCS (B = +4.69), with a positive interaction term (AB = +7.5476). This indicates that higher binder levels—and certain A:B combinations—produce more compact tablets with greater mechanical strength, consistent with the expected role of PVP K30 in enhancing inter-particle bonding and compressibility.

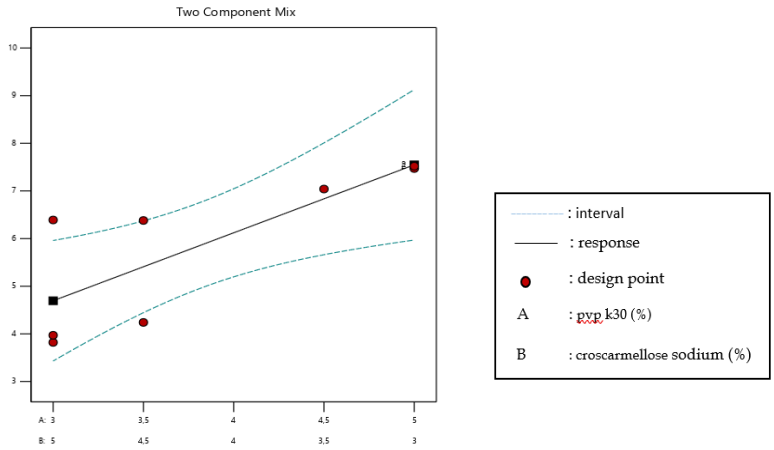

Figure 2. Contour plot of tablet hardness (kp) versus PVP K30 (A) and croscarmellose sodium (B); target 4–8 kp is highlighted

For friability (**Figure 3**), coefficients are A = +0.198, B = +0.576, and AB = −0.202. Thus, increasing CCS tends to raise friability more than PVP K30 does, while the negative AB term suggests that appropriate A:B combinations can mitigate friability relative to a simple linear blend—matching the experimental finding that higher-binder mixtures achieve lower % mass loss within the <1% acceptance limit [17].

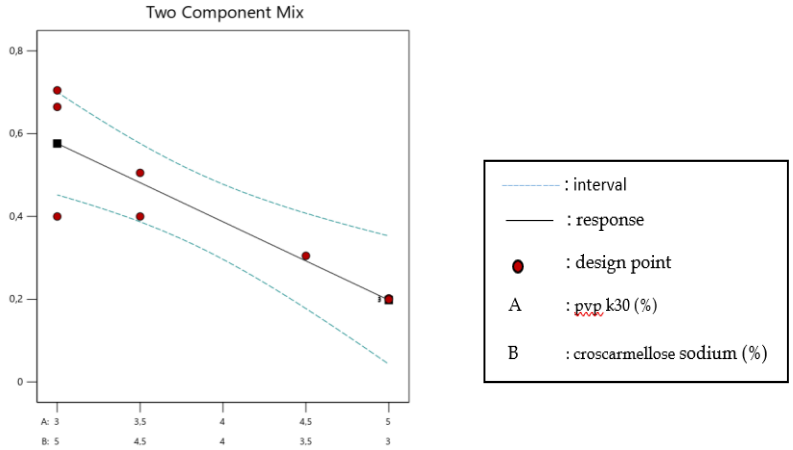

Figure 3. Contour plot of tablet friability (%) versus PVP K30 (A) and croscarmellose sodium (B); limit <1% is highlighted

For disintegration (Figure 4), the response is correctly labelled "Disintegration time (s)" (the SLD analysis used seconds; values may be reported as mm:ss elsewhere). The fitted coefficients (A = 478.49; B = 201.46; AB = +478.48) indicate that increasing PVP K30 lengthens disintegration (stronger compacts slow water ingress), whereas increasing CCS shortens disintegration via wicking/swelling. The positive AB term slightly increases the predicted time relative to a purely linear blend, i.e., it is antagonistic to very rapid disintegration when both excipients are high. These response-surface patterns (**Figures 2–4**) are consistent with the experimental tables reported above and define the optimisation window used later to identify formulations that simultaneously satisfy all three specifications [17],[18].

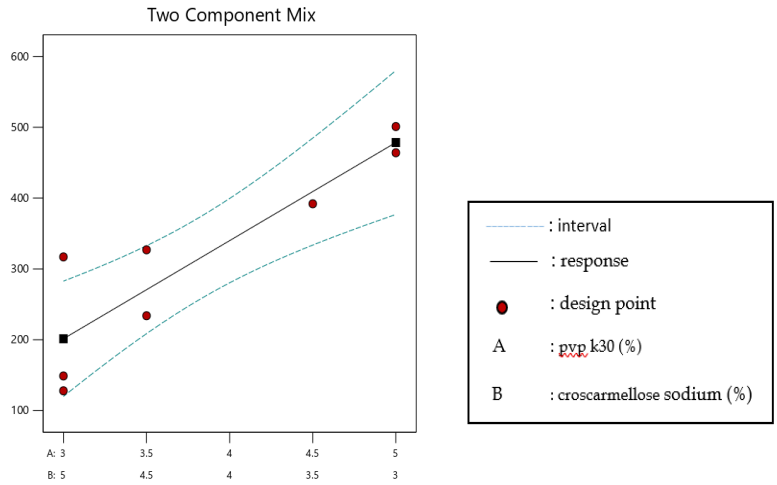

Figure 4. Contour plot of tablet disintegration time versus PVP K30 (A) and croscarmellose sodium (B); limit <15 min is highlighted

Determination of the Optimum Formulation

Multi-response optimisation was performed in Design-Expert v13 using the numerical desirability function to satisfy the three preset quality targets simultaneously—hardness 4–8 kp [18], friability <1%, and disintegration <15 min [17]. In this approach each response is first transformed to a unitless desirability, and the overall score (geometric mean) is maximised so that a higher desirability reflects a better compromise across responses within the mixture space A = PVP K30 and B = croscarmellose sodium (CCS) (A + B = 1) [13].

Table 8. Optimisation summary (Design-Expert v13; numerical desirability)

Factor/Response	Predicted value	Spec/Target
PVP K30 (A)	5.0%	–
CCS (B)	3.0%	–
Hardness (kp)	7.55	4–8 kp [18]
Friability (%)	0.198	< 1% [17]
Disintegration time	07:58 (mm:ss)	< 15 min [17]
Desirability	1.00	maximise

The optimiser returned a single solution with desirability = 1.00 at 5% PVP K30 : 3% CCS, with predicted responses hardness 7.55 kp, friability 0.198%, and disintegration 07:58 (**Table 8**). The corresponding overlay/contour plot (**Figure 5**) shows that this composition lies inside the feasible region where all three specifications—hardness 4–8 kp, friability <1%, disintegration <15 min—are met concurrently [17],[18]. This location is consistent with the response-surface trends described earlier (**Figures 2–4**): increasing PVP K30 strengthens compactibility (hardness ↑, friability ↓), whereas increasing CCS accelerates breakup (disintegration time ↓).

Table 9. Evaluation of the optimal formulation (three independent batches)

Evaluation	Batch 1	Batch 2	Batch 3	Mean ± SD
Weight uniformity (CV, %)	0.90	1.03	0.97	0.96 ± 0.06
Thickness (cm) ± SD	0.46 ± 0.03	0.47 ± 0.06	0.48 ± 0.05	0.47 ± 0.01
Diameter (cm) ± SD	1.25 ± 0.00	1.25 ± 0.00	1.25 ± 0.00	1.25 ± 0.00
Hardness (kp) ± SD	6.27 ± 0.54	6.23 ± 0.58	6.34 ± 0.91	6.28 ± 0.05

Friability (%) ± SD	0.17 ± 0.006	0.18 ± 0.007	0.16 ± 0.01	0.17 ± 0.01
Disintegration (mm:ss)	06:52 (range 06:14–07:32)	06:42 (range 06:12–07:33)	06:57 (range 05:20–07:45)	06:50 ± 0.07 min

To verify the model, the optimal composition was manufactured in triplicate (200 tablets per batch) and evaluated for routine quality attributes (**Table 9**). All batches complied with pharmacopoeial expectations: weight CV 0.96%, thickness 0.47 cm and diameter 1.25 cm, hardness 6.28 ± 0.05 kp, friability 0.17 ± 0.01%, and disintegration 06:50 ± 0.07 min, all within the respective limits of 4–8 kp, <1%, and <15 min [17],[18]. These data indicate that the laboratory process reliably reproduces tablets that meet the multi-attribute target profile at the selected point.

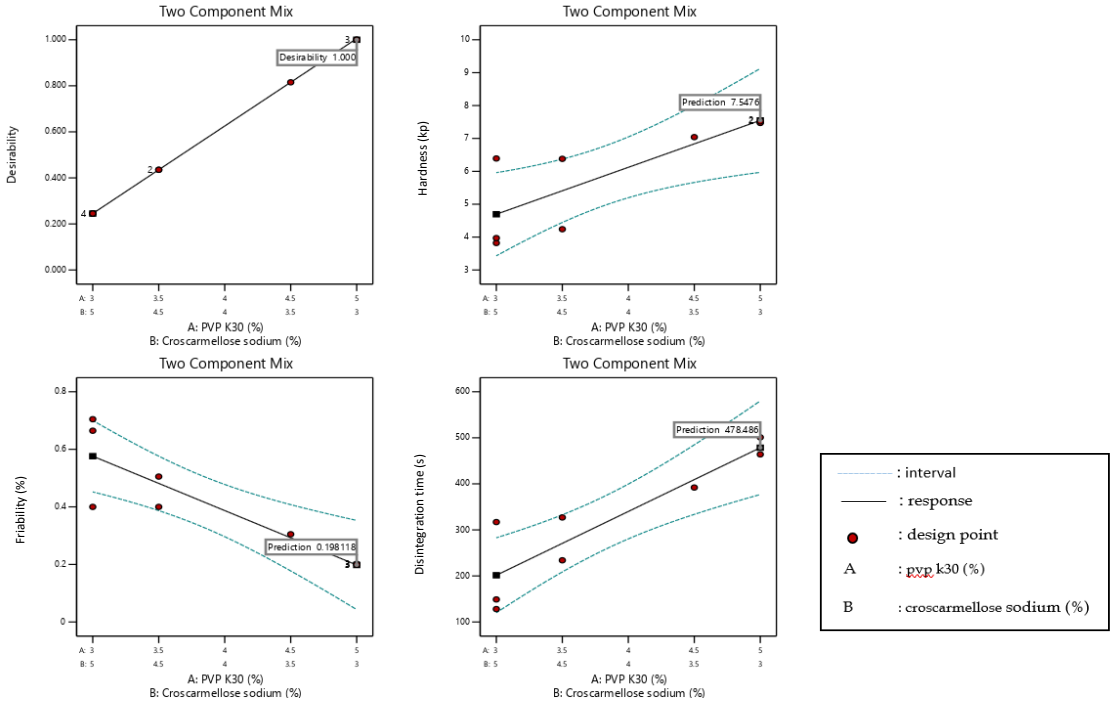

Figure 5. Prediction and desirability profiles for the two-component mixture (A = PVP K30, B = croscarmellose sodium/CCS) showing desirability, hardness (kp), friability (%), and disintegration time (s). The optimal point (5% PVP K30, 3% CCS; desirability = 1.00) and 95% prediction intervals are indicated

Observed means were then compared with the point predictions and prediction ranges from Design-Expert (**Table 10**). For hardness, the observed mean (6.28 kp) was slightly lower than the point prediction (7.55 kp) but remained inside the prediction interval (5.96–7.61 kp) and within the 4–8 kp specification; friability and disintegration were equal to or better than predicted and likewise within their intervals (0.043–0.353% and 06:26–09:40, respectively). Collectively, this confirms the adequacy and robustness of the optimisation and supports the use of 5% PVP K30 : 3% CCS as the working formulation under routine processing [13],[17],[18].

Table 10. Verification of the optimal formulation against model predictions

Response	Predicted	Prediction range	Observed (mean ± SD)	Meets spec
Hardness (kp)	7.55	5.96–7.61	6.28 ± 0.05	Yes (4–8 kp)
Friability (%)	0.198	0.043–0.353	0.17 ± 0.01	Yes (< 1%)
Disintegration (mm:ss)	07:58	06:26–09:40	06:50 ± 0.07 min	Yes (< 15 min)

From a formulation-mechanistic perspective, the chosen point reflects the expected binder–superdisintegrant trade-off: PVP K30 strengthens inter-particle bonding and increases compactness, which raises hardness and reduces friability, whereas CCS facilitates rapid fluid ingress and matrix swelling, which shortens disintegration time—patterns also reported in related systems using CCS with PVP-based binders [7],[20]. Importantly, the optimum provides comfortable margins against all limits (friability well below 1%, disintegration at roughly half of the 15-minute limit, and hardness near the mid-range), thereby reducing the risk of out-of-specification results under normal batch-to-batch variability [17],[18].

This work had several practical constraints. First, maintaining process consistency during wet granulation and compression was challenging; small variations in mixing time and compression force can measurably affect hardness, friability, and disintegration, introducing batch-to-batch variability. Second, laboratory capacity limited the scope of testing: we did not perform dissolution or long-term stability studies, so in-vitro release behaviour and stability under real/accelerated conditions remain uncharacterised. Third, the optimisation space was intentionally narrow—restricted to two mixture factors (PVP K30 and CCS) within predefined ranges—so potential improvements outside this window were not explored within the present study.

4. Conclusion

This study set out to identify a PVP K30–croscarmellose sodium balance that yields adequate mechanical strength together with rapid disintegration. Using a Simplex sattice design, the optimal composition was 5% PVP K30 and 3% croscarmellose sodium, which—when manufactured in triplicate—produced tablets with hardness 6.28 ± 0.05 kp, friability 0.17 ± 0.01%, and disintegration 06:50 ± 0.07 min (range 05:20–07:45). These values meet the predefined specifications (hardness 4–8 kp, friability <1%, disintegration <15 min), confirming that the objective was achieved. This work focused on physical quality attributes. Future studies should extend the evaluation to include dissolution profiles, chemical/physical stability, and, where feasible, pharmacological activity or biorelevant release, and may explore broader excipient ranges to further optimise performance and support scale-up.

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Conflicts of Interest:

The author declares that there are no conflicts of interest in this research.

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