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Research Article

Formulation of Effervescent Granules Based on *Calotropis procera* Ait Powder. (Apocynaceae) and *Zanthoxylum zanthoxyloides* Lam. (Rutaceae)

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Abstract

Introduction: Sickle cell disease is a genetic disease that affects nearly 5% of the world's population and is particularly prevalent in sub-Saharan Africa. The inaccessibility of modern treatment has led to the development of a phytomedicine called FACA® in Burkina Faso. It is formulated in capsule form and contains a mixture of powdered root barks of *Zanthoxylum zanthoxyloides* and *Calotropis procera*. This study aims to propose an alternative, easier-to-administer form for patients who have difficulty swallowing capsules by developing effervescent granules. Materials and methods: Pre-formulation studies focused on analyzing the physicochemical and pharmaco-technical properties of the powder mixture. These included macroscopic and organoleptic aspects, pH, residual moisture content, hygroscopicity, granulometry, and flow. Effervescent granules were formulated and manufactured by the wet granulation method. Five formulations (F1-F5) were produced. Citric acid and sodium bicarbonate were used as effervescent vehicles at a ratio of 1:1.25. PVP was used as a binding agent, sucrose as a sweetener, and cornstarch as a diluent. The granulation liquid was distilled water. The granules produced were evaluated for their physicochemical properties and disintegration time. Results and discussion: the results of the physicochemical and pharmaco-technical characteristics guided the choice of excipients and the manufacturing process. The formulations were beige in color and granular in appearance. THR values were <10%, pH ranged from 5.20 ± 0.29 to 5.91 ± 0.17. They were more or less hygroscopic and presented good rheological properties with an effervescence time satisfying the specifications of the European Pharmacopoeia 11th edition. Conclusion: F4 formulation had the best characteristics and could serve as an alternative to capsules. Indeed, being dispersed in water before administration, these granules could be well tolerated by the gastrointestinal tract and promote a more rapid action of the drug at a time of crisis.

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Keywords

Sickle Cell Disease, Herbal Medicine, Formulation, Granules, Effervescent, *Zanthoxylum zanthoxyloides*, *Calotropis procera*

1. Introduction

FACA® is a herbal medicine containing a mixture of powdered root barks of *Zanthoxylum zanthoxyloides* Lam. (Rutaceae) Zepernick, Timler and *Calotropis procera* (Ait.) R. Br. (Apocynaceae). It is manufactured by the production unit of the Institut de Recherche en Sciences de la Santé (IRSS) in Burkina Faso.

Scientific studies from laboratory work (*in vitro* and *in vivo*) have highlighted the therapeutic properties of this phytomedicine. Chemical studies have identified divanilloylquinic acids (Burkinabines A, B, and C) from the root bark of *Z. zanthoxyloides*, whose anti-sickling properties have been demonstrated [1]. Other studies have demonstrated the anti-inflammatory and analgesic properties of *C. procera* extracts. The combination of two plants would act in synergy in the improvement of crises in sickle cell patients thanks to the several pharmacological properties including those antifalciform, analgesic, antipyretic, anti-inflammatory, myorelaxant and spasmogenic and vasodilatory highlighted [2]. A comparative pharmacological study between dihydroergotoxin on the one hand, and FACA® on the other hand carried out in children with sickle cell crisis confirmed its efficacy [3]. The results of these preclinical and clinical studies have made it possible to consider the industrial production of this phytomedicine. First produced in capsule form, it obtained marketing authorization (MA) in 2010 and was included on the list of essential medicines in Burkina Faso in 2011 [4]. Since then, much work has been undertaken to develop other galenic forms of this phytomedicine suitable for the characteristics of the disease and the patients. A study of standardization of the raw material was carried out, resulting in the development of a pediatric form (powder for oral suspension) [5]. This form is in a clinical trial phase. This research work focuses on the development of effervescent granules for the advantages that they offer. Indeed, for some patients who have difficulty swallowing tablets and capsules, this oral dosage form is a good alternative. Being previously dissolved, effervescent products do not come into direct contact with the gastrointestinal tract. They can therefore be well tolerated by the stomach and intestines [6]. In terms of pharmaceutical quality, they have better physical stability, good solubilization, and good conservation [7]. Technologically, they exhibit better flowability, greater stability, better wetting, and greater uniformity in particle size, and therefore in drug content, than powders [8].

2. Materials and Methods

2.1. Materials

The mixture of powders of root barks of *Zanthoxylum zanthoxyloides* and *Calotropis procera* was supplied to the U-PHARMA production unit of the IRSS (Burkina Faso). Excipients consisting of Citric Acid powder (lot A0405191), were purchased from ACROS Organics (Austria), Sodium Bicarbonate powder (lot 20230216), Henan Zhongyan Chemical Co. Ltd (China); Povidone powder (PVP): lot 18D3056932, VWR Chemicals, LLC (USA); Sucrose, Corn Starch were purchased from Sigma Aldrich (UK). Solvents, such as Ethanol, Methanol, and Chloroform were purchased from Fischer Scientific (UK).

2.2. Methods

2.2.1. Pre-formulation Study

(i). Macroscopic and Organoleptic Characteristics

The macroscopic characteristics observed were texture and color. The texture was determined by pinching the powder between the fingers and color by comparing the powder mixture to a color dictionary. The organoleptic characteristics (taste and odor) were determined by tasting and sniffing the powder.

(ii). Residual Moisture Content

The residual moisture content (RMC) of the powder was determined using the thermogravimetric method. One (01) g of the powder was placed in a moisture analyzer balance whose drying temperature was set at 105°C. The result was read after 15 min. The test was carried out in triplicate and the mean and standard deviation were calculated.

(iii). Hygroscopicity

Hygroscopicity was determined according to the method described in the European Pharmacopoeia 10th edition [9]. One (1) g of powder was weighed and placed in an oven at 105°C for 1h30mn. The dried powder was then introduced into a suitable desiccator containing a previously prepared saturated solution of ammonium chloride for 24 hours. The percentage mass increase was calculated using the expression:

$$M = \frac{m3 - m2}{m2 - m1} \times 100$$

m1: mass of the container
m2: mass of the container plus powder at T0 hour
m3: mass of the container plus powder at T 24 hours

The test was performed in triplicate and the mean with standard deviation was calculated. The result was interpreted according to the specifications of the European Pharmacopoeia 11th edition [10].

(iv). pH

The pH was determined by dipping the pH meter electrode into 1% (m/v) aqueous solutions of the powder. The test was performed in triplicate and the mean and standard deviation were calculated (m± standard deviation, n = 3).

(v). Solubility

The solubility of the powder was determined according to the procedure described in the European Pharmacopoeia 10th edition [9]. Four (04) solvents were used: distilled water, ethanol, methanol, and chloroform.

(vi). Granulometry

It was determined by the sieve method described in the European Pharmacopoeia 10th edition [9]. A mass of 50g of powder was introduced into the upper sieve of a column of ten (10) sieves with mesh openings of 1; 0.9; 0.71; 0.63; 0.5; 0.4; 0.25; 0.16; 0.1 and 0 mm, placed on a vibrator. The vibrator was operated at an amplitude of 50 vibrations per minute for 5 minutes. The sieves were then removed and weighed to determine the mass of rejects in each sieve. The average diameter of the powder was also calculated.

(vii). Flow

The flow time, angle of repose, Carr index, and Hausner ratio were determined according to the procedures of the European Pharmacopoeia 10th edition [9].

1. The Angle of Repose: The powder was introduced through a funnel attached to a metal support to form a cone on a horizontal surface. The height and diameter of the cone were measured and the angle of repose was calculated using the expression:

$$\text{Tan } \propto = \text{hauteur}/(0{,}5 \times \text{base})$$

The result was interpreted according to the flowability scale as a function of the angle of repose.

2. The Carr index and Hausner ratio: The Carr index and Hausner ratio of the powder were determined by measuring the apparent untamped volume and then the final volume after tamping until a constant volume was obtained according to the method described in the European Pharmacopoeia 10th edition [9]. They are defined by the following expressions:

$$\text{Carr index} = 100X\ (V0-Vf)/V0$$

$$\text{Hausner index} = V0/Vf$$

The sieves were then removed and weighed to determine the mass of rejects in each sieve. The average diameter of the powder was also calculated.

2.2.2. Formulation of Effervescent Granules

(i). Determination of the Ratio of Effervescent Agents

Inspired by the method of Adi-Dako et al. [11], preliminary tests between citric acid and sodium bicarbonate were carried out to determine the optimal ratio for the formulations. For this, from 50g of citric acid, different proportions of sodium bicarbonate were added (Table 1) to constitute an acid-base mixture which was then dissolved in water. The disintegration time, pH, and solubility of the mixture were evaluated. The ratio that gave the best results for these parameters was retained for the different formulations.

Table 1. *Determination of acid-base ratio.*

Test	Citric acid (mg)	Sodium bicarbonate (mg)	Ratio
E1	50	200	1:4
E2	50	175	1:3.5
E3	50	150	1:3
E4	50	125	1:2.5
E5	50	100	1:2
E6	50	62.5	1:1.25
E7	50	50	1:1

(ii). The Manufacturing Process for Effervescent Granules

The effervescent granules were produced by the wet granulation method. The weighing was carried out on a clean bench and using a calibrated analytical balance. The label of each product was checked before weighing. The powders were ground in a mortar and sieved using a 500µm sieve to ensure a homogeneous mixture. The mixture was then mixed with a sufficient quantity of distilled water until a mass of suitable consistency for granulation was obtained. Granulation was carried out using an oscillating granulator on which a 1.24 mm mesh screen was mounted. The mass to be granulated was gradually introduced into the running granulator. The granules were collected on a sheet of paper placed below the device then spread out and dried in an oven. The dry granules were finally calibrated to retain grains of size between 1mm and 0.5mm before being packaged in single-dose sachets of 80mg of vegetable powder.

(iii). Qualitative and Quantitative Formulation

These formulations were intended to determine the influence of the quantity of effervescent agents on the characteristics of effervescent granules. For this, five (05) formulations (F1-F5) were produced. Comparing the formulations to the case of effervescent tablets, the proportion of sodium bicarbonate has evolved between 20 and 40% [12]. The proportion of acid was calculated from that of bicarbonate for a ratio of 1:1.25 respectively. PVP was used as a binder, sucrose as a sweetener, and starch as a diluent. The quantitative formulation is given in Table 2.

Table 2. *Determination of acid-base ratio.*

Composition (%)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)
Vegetable powder	5	5	5	5	5
citric acid	16	20	24	28	32
Na bicarbonate	20	25	30	35	40
PVP	4	4	4	4	4
Sucrose	15	15	15	15	15
Corn starch	40	31	22	13	4

(iv). Quality Control of Effervescent Granules

The granules produced were evaluated for their macroscopic characteristics, RMC, hygroscopicity, pH, and particle size, following the same methods used for vegetable powder.

Granule flow was evaluated by measuring flow time and determining the angle of repose, Carr index, and Hausner ratio. The Carr index and the Hausner ratio were calculated from the apparent and tapped density of the granules according to the expressions:

$$\text{Carr index}=100X\ (\rho\text{tasse}-\rho\text{vrac})/\rho\text{vrac}$$

$$\text{Hausner index}=\rho\text{tasse}/\rho\text{vrac}$$

The disintegration time was also evaluated for the different formulations following the procedure indicated in the European Pharmacopoeia 10th edition [9]. An amount equivalent to one dose of granules of each formulation was introduced into a beaker containing 250 mL of distilled water. The effervescence time was measured using a stopwatch.

3. Results

3.1. Pre-Formulation

3.1.1. Macroscopic and Organoleptic Characteristics

The powder used was brownish (Figure 1). The texture was slightly fine with a somewhat characteristic odor. It had a bitter and slightly spicy taste.

Figure 1. *Appearance of the powder.*

3.1.2. RMC, pH, and Hygroscopicity

The results of the evaluation of RMC, pH, and hygroscopicity of the powder are given in Table 3.

Table 3. *Results of RMC, pH, and Hygroscopicity of the powder.*

Parameter studied	Results
RMC	7.29% ±0.1
pH	5.94 ± 0.01
Hygroscopicity	13.92 ± 0.5

3.1.3. Solubility

The vegetable powder was insoluble in the four (04) solvents used in this study.

3.1.4. Powder Particle Size

The results of the granulometric analysis of the powder made it possible to draw a curve representing the percentage of rejects in each sieve (Figure 2). The cumulative rejection of the 0, 0.1, and 0.16 mm sieves was 54.47%. The calculated average diameter was 240.14 µm.

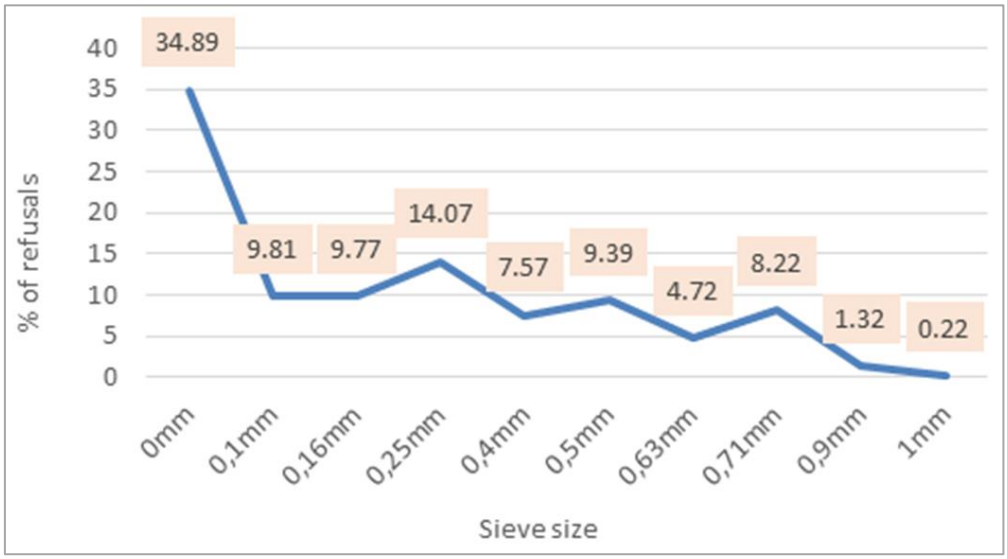

Figure 2. *Representative curve of the percentages of powder rejection in the sieves.*

3.1.5. Powder Flow

The rheological characteristics of the powder are presented in Table 4.

Table 4. *Rheological characteristics of the powder.*

Settings	Flow time	Angle of repose	Carr Index	Hausner ratio
Results	Infinite	39.5°	30.83%	1.44

3.2. Acid-base Ratio

Determination of the ratio between citric acid and sodium bicarbonate gave the results in Table 5.

Table 5. *Results of the test between citric acid and sodium bicarbonate.*

Formulation	Ratio	Citric acid (mg)	Sodium bicarbonate (mg)	Time of effervescence (s)	pH	Solubility
E1	1:4	50	200	25	7.1	Slightly soluble
E2	1:3.5	50	175	32	7.2	Soluble
E3	1:3	50	150	36	7.2	Soluble
E4	1:2.5	50	125	45	7.1	Soluble
E5	1:2	50	100	55	7.0	Readily soluble
E6	1:1.25	50	62.5	70	6.9	Very soluble
E7	1:1	50	50	65	6.9	Very soluble

The ratio of 1:1.25 respectively for citric acid and sodium bicarbonate gave the best effervescence time (70s) with very good solubility and a pH of 6.9. This ratio corresponds more or less to the stoichiometry of the reaction. Indeed, the stoichiometric calculation gives a ratio of 1:1.2 for citric acid and base respectively [13].

3.3. Quality Control of Effervescent Granules

3.3.1. Macroscopic and Organoleptic Characteristics

The granules of all formulations had a more or less beige color with a granular texture (Figure 3). The taste was more or less sour and spicy.

Figure 3. *Appearance and color of effervescent granules.*

3.3.2. Macroscopic and Organoleptic Characteristics

The RMC and pH values of the different formulations are shown in Table 6. All formulations had an RMC between 2.20 and 3.54.

The pH ranged from 5.20 ± 0.29 for F5 to 5.91 ± 0.17 for F4.

The determined hygroscopicity ranged from 0.94 ± 0.28 (F5) to 10.63 ± 0.22 (F1).

Table 6. *RMC, hygroscopicity, and pH values of the formulations.*

Formulation	F1	F2	F3	F4	F5
RMC	3.54 ± 0.19	2.93 ± 0.08	2.53± 0.27	2.39 ± 0.03	2.20 ± 0.21
Hygroscopicity	10.63±0.22	9.72 ± 0.16	5.59 ±0.16	4.39 ± 1.08	0.94 ±0.28
pH	5.55± 0.61	5.65 ± 0.66	5.25 ± 0.20	5.91 ± 0.17	5.20 ± 0.29

3.3.3. Granulometry

The results of the sieve rejection percentage of the five formulations are shown in Figure 4. The average granule diameter of these formulations was 621.06 for F1, 730.96 for F2, 712.21 for F3, 755.28 for F4, and 832.44 for F5.

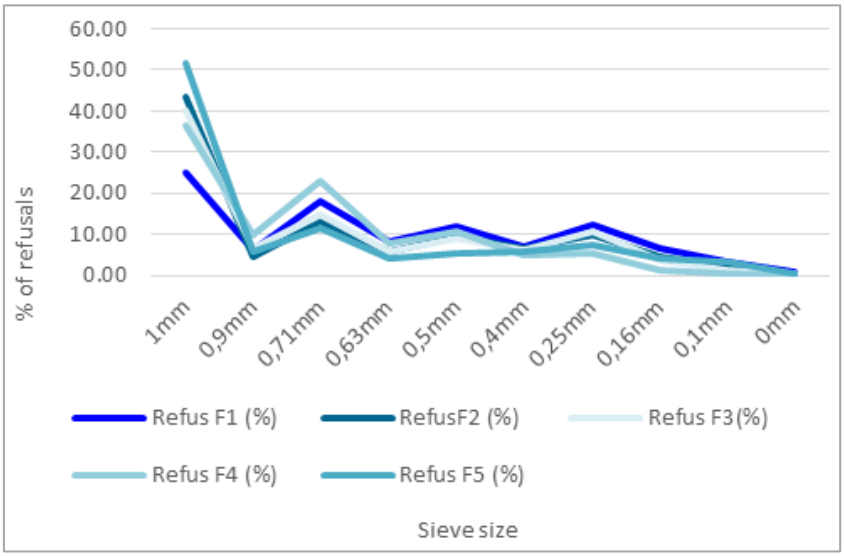

Figure 4. *Representative curves of the sieve rejection percentages of the different formulations.*

3.3.4. Loss Rate After Screening

Post-screening evaluation of each formulation gave the results shown in Table 7.

Table 7. *Percentage (%) of loss after screening.*

Pellets (g)	M1	M2	LOSS	% LOSS
F1	58.36	38.21	20.15	34.53
F2	56.21	40.88	15.33	27.27
F3	55.2	45.8	9.4	17.03
F4	56.75	51.84	4.91	8.65
F5	54.7	44.08	10.62	19.41

3.3.5. Flow of Pellets

The determination of the angles of repose, the apparent and packed densities as well as the Carr indices and Hausner ratio of the granules gave the results which are presented in Table 8.

Table 8. *Pellet flow test results.*

Formulations	Angle of repose	Apparent density	Packed Density	Carr index	Hausner's report
F1	17.97 ± 0.4	0.48 ± 0.01	0.54 ± 0.02	12% ± 0.02	1.13 ± 0.03
F2	18.07 ± 0.74	0.48 ± 0.01	0.52 ± 0.02	09% ± 0.01	1.02± 0.00
F3	18.71± 0.92	0.42 ± 0.01	0.48 ± 0.01	13% ± 0.01	1.14 ± 0.01
F4	18.66 ± 0.30	0.50 ± 0.02	0.57 ± 0.01	13% ± 0.02	1.15 ± 0.02
F5	17.5 ± 0.9	0.42 ± 0.00	0.44 ± 0.01	05% ± 0.02	1.05 ± 0.02

3.3.6. Disintegration Time

The disintegration time of the different formulations, estimated by stopwatch, is given in Table 9.

Table 9. *Granule disintegration time.*

Formulations	F1	F2	F3	F4	F5
Time (s)	8.67 ± 1.53	15.33 ± 2.08	27 ± 2	33.67 ± 1.53	42 ± 3

4. Discussion

Evaluation of the macroscopic and organoleptic characteristics revealed that the powder had a brown color. It had a slightly fine texture with a slight characteristic odor and a bitter, slightly pungent taste. This description of the powder is close to that given by Ouédraogo et al. [4] who found that the powder contained white and brown particles, a little odorous, bitter with the sensation of tingling and anesthesia on the tongue. These parameters could be used for the identification of plant powder during formulations.

The RMC of the powder was 7.29% ±0.1. This content, less than 10%, is a favorable criterion for its conservation. Indeed, a high residual moisture content (≥10%) could promote certain enzymatic reactions that can lead to an alteration of the appearance of the substances, their organoleptic properties, and even their therapeutic virtues [9]. High humidity is also favorable to the development of microorganisms. The result obtained is close to that of Ouédraogo et al. who found an RMC of 8.01 ±0.06 [4].

The hygroscopicity test of the powder gave a value of 13.92% ±0.5. This value, which represents the increase in mass, is between 2% and 15%. The powder could therefore be described as hygroscopic according to the specifications of the European Pharmacopoeia. This means that the dry powder could absorb moisture from the air during handling and storage. Hence the need to store it in airtight containers and to carry out handling in areas with controlled humidity.

The solubility test showed that the plant powder was neither soluble in distilled water nor methanol, acetone, and chloroform. Knowledge of the solubility of the herbal drug could guide the choice of excipients in the formulation. The active substance must be soluble, dispersible in water, or at least solubilized by the formation of salts when dissolved in a glass of water [14]. As noted by Adi-Dako et al, several herbal products, despite their exceptional therapeutic potential, have limited or reduced therapeutic action due to their low aqueous solubility [11]. However, in the case of effervescent granules, the solubility or dispersion in water could be improved by the "bursting" effect caused by the effervescent agents.

The particle size analysis of the powder showed that it was not homogeneous. It could be described as moderately fine according to the specifications of the European Pharmacopoeia. Also, more than 50% of the powder had a size between 0 and 250 µm. The average diameter calculated is 240.14 µm. The study by Ouédraogo et al. found a cumulative refusal of 64.38% on the 200 µm sieve [4]. The fineness of the powder could partly influence its flow. The rheological study also revealed that it had poor flow based on the angle of repose, the Carr index, and the Hausner ratio. Indeed, many powders, due to their small size, irregular shape, or surface characteristics, are cohesive and do not flow well [15]. The rheological study also revealed that it had poor flow based on the angle of repose, the Carr index, and the Hausner ratio. Granulation would improve the flow of this powder.

The effervescent granules containing FACA® powder have been formulated by the wet granulation method.

To determine the ratio of effervescent agents, a series of tests between citric acid and sodium bicarbonate were carried out. The ratio of 1:1.25 for citric acid and sodium bicarbonate respectively was retained as the best ratio based on effervescence time, pH value, and solubility. This roughly corresponds to the stoichiometric calculation of the reaction which gives a ratio of 1:1.2 for citric acid and base respectively [13]. Additionally, several effervescent granule formulation studies using both citric and tartaric acids have employed similar ratios of 1:2:3.4 for citric acid, tartaric acid, and sodium bicarbonate respectively [7, 11, 16]. This allowed the testing of the five formulations (F1-F5) of effervescent granules with different proportions of effervescent agents to determine the optimal quantities of effervescent agents.

The pellets of all five formulations were beige in color and very granular in texture.

All formulations had a THR between 2.20% and 3.54%. These low percentages show that the pellets were quite dry and could be packaged with a low risk of microorganism development and degradation. Generally speaking, a humidity level between 3% and 5% is often considered optimum [17].

The pH ranged between 5.20 ± 0.29 and 5.91 ± 0.17 for F5 and F4 respectively. These values which are close to the pH of the vegetable powder (especially F4) could constitute a guarantee of its stability in the formulations. It was less than 6 in all formulations after effervescence. Jassim et al. also found in their formulation of effervescent granules pH < 6 and observed that this could be due to the release of CO_2 and the consumption of sodium bicarbonate [18].

The determined hygroscopicity was between 0.94±0.28 (F5) and 10.63±0.22 (F1). This decrease in hygroscopicity percentages could be attributed to the powder being classified as hygroscopic according to the specifications of the European Pharmacopoeia or the effect of corn starch. Indeed, according

to the Handbook of Pharmaceutical Excipients, sixth edition [12], the latter is hygroscopic and easily absorbs atmospheric humidity. It absorbs up to 12% for a relative humidity of 50%. Thus, a high proportion of this excipient in the formulation may compromise its quality and stability. Given this parameter, this type of preparation requires airtight packaging. It would be preferable to package the effervescent granules in single-dose sachets.

The representative curves of the granulometric analysis of the different formulations showed a similarity in the evolution of the percentages of rejections by sieve. The cumulative rejections of the 1mm, 0.9mm, 0.71mm, 0.63mm, and 0.5mm sieves gave 87.82% for F4. This value is higher than the rest of the formulations. Also, the screening carried out gave a better yield for F4, i.e. only a loss of 8.65%. This difference could be explained by the low proportion of corn starch. Corn starch, which also acts as a disintegrant [13] could contribute to increasing the friability of the granules. The fact that F5 has a low yield compared to F4 while having a lower amount of starch could be attributed to the formulation process.

The apparent density ranged from a minimum of 0.42±0.00 g/ml to a maximum of 0.50±0.02 g/ml, indicating an average of 3.2-3.8 ml apparent volume per 1.6 g of granules. This volume is suitable for unit dose packaging. These values are close to those of Bhattacharyya et al. who had obtained for their formulation, apparent densities of 0.54±0.01 gm/ml to 0.66±0.01 g/ml with 1.5-2 mL of volume per gram of granules [8].

Evaluation of flow characteristics showed that granules of all formulations flowed very quickly in less than 5 seconds. The angles of repose of all formulations were less than 20°C, corresponding to excellent flow. Similarly, the values of the Carr index and the Hausner ratio show that the granules have good flow.

These values indicate that the granules to be used have good flow properties and that optimum filling will be obtained when manufacturing fixed-dose sachets [13].

The disintegration time of the granules of the 5 formulations was between 8s and 42s. It is almost instantaneous for F1 where the proportion of effervescent agents was only 36%. This time was increasingly marked by the increase in the proportion of effervescent agents. All five formulations had a disintegration time of less than 5 min, indicating that they met the disintegration test for effervescent granules according to European Pharmacopoeia 11.0 [10]. Bhattacharyya et al had obtained effervescence times of less than 20 seconds [8]. Al-Mousawy et al had found for their formulation effervescence times between 80 and 113 seconds [7] for their effervescent granules. It was remarkable that the higher the proportion of effervescent agents in the formulation, the more marked the effervescence. The disintegration was also accompanied by foam formation which was more marked for F5. Of the five formulations produced, formulation F4 could be considered the best. Indeed, it presented the lowest RMC (2.09 ± 0.03), its pH was closest to neutrality (5.91 ± 0.17), and a larger grain size (755.28µm) with a good yield after screening. It presented an excellent flow and a good disintegration time.

5. Conclusions

The objective of this study was to develop effervescent granules based on FACA® powder. The study of the characteristics of powder guided the choice of excipients for the formulation. The granules were prepared by wet granulation technique with citric acid and sodium bicarbonate as effervescent agents at the ratio of 1:1.25 respectively. The formulated granules gave satisfactory results about physicochemical and pharmacotechnical properties. Formulation F4 was selected as the best formulation. This galenic form will serve as an alternative with the advantage of ease of administration and promoting acceptability in patients who have difficulty swallowing capsules. They would also promote rapid action of the drug and would be beneficial in times of crisis.

Abbreviations

RMC Residual Moisture Content

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Author Contributions

Ouédraogo Salfo: Conceptualization, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing

Atchadé Boladé Constantin: Investigation, Methodology, Project administration, Software, Writing – original draft

Traoré Tata Kadiatou: Conceptualization, Formal Analysis, Funding acquisition, Methodology, Project administration, Resources, Software, Validation, Visualization, Writing – original draft, Writing – review & editing

Rouamba Téyindé Songré Martin: Conceptualization, Investigation, Methodology, Validation

Traoré Safiatou: Conceptualization, Investigation, Methodology, Validation

Goumbri Wendinmi Bertrand Florent: Investigation, Methodology, Resources, Software, Validation

Yaméogo Boumbéwendin Gérard Josias: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Supervi-

sion, Validation, Visualization

Ouédraogo Sylvin: Conceptualization, Investigation, Visualization

Semdé Rasmané: Conceptualization, Funding acquisition, Validation, Visualization

All authors contributed similarly to manuscript writing, literature research, review design, literature analysis, and final text approval.

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Data Availability Statement

The authors declare that all the supporting data are contained within the paper.

Conflicts of Interest

The authors declare no conflicts of interest.

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